L Number	Hits	Search Text	DB	Time stamp
1	338	proanthocyanidin	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:19
2	94	proanthocyanidin and (isolation or purification)	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:20
3	64	(proanthocyanidin and (isolation or purification)) and chromatography	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:20
4	52	((proanthocyanidin and (isolation or purification)) and chromatography) and (anionic or silica or octadecyl or phenyl)	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 14:04
5	0	(((proanthocyanidin and (isolation or purification)) and chromatography) and (anionic or silica or octadecyl or phenyl)) and ribosylation	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:26
6	2	proanthocyanidin and ribosylation	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:47
7	0	proanthocyanidin and enterotoxin	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 13:48
9	45	(proanthocyanidin and (apple or grape)) and (isolation or purification)	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 14:10
10	15	((proanthocyanidin and (apple or grape)) and (isolation or purification)) and (tetramer and higher)	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 14:08
8	131	proanthocyanidin and (apple or grape)	USPAT; US-PGPUB; EPO; DERWENT	2002/11/21 14:11

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NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28	Oct 21	EVENTLINE has been reloaded
NEWS 29	Oct 24	BEILSTEIN adds new search fields
NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 32	Nov 18	DKILIT has been renamed APOLLIT

NEWS EXPRESS	October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:34:15 ON 21 NOV 2002

=> index chemistry
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

INDEX 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...'
ENTERED AT 14:34:43 ON 21 NOV 2002

46 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view search error messages that display as 0* with SET DETAIL OFF.

=> s proanthocyanidi
45 FILES SEARCHED...

0 FILES HAVE ONE OR MORE ANSWERS, 46 FILES SEARCHED IN STNINDEX

L1 QUE PROANTHOCYANIDI

=> s proanthocyanidin

398	FILE AGRICOLA
68	FILE ANABSTR
4	FILE APOLLIT
223	FILE BABS
1	FILE BIOCOMMERCE
105	FILE BIOTECHNO
671	FILE CABA
11	FILE CAOLD
2046	FILE CAPLUS
11	FILE CBNB
12	FILE CEABA-VTB
2	FILE CEN
4	FILE CIN
17	FILE COMPENDEX
20	FILE CONFSCI
2	FILE ENCOMPLIT
2	FILE ENCOMPLIT2
17	FILE FEDRIP
8	FILE GENBANK
3	FILE INVESTEXT
32	FILE IPA
96	FILE JICST-EPLUS
8	FILE KOSMET
249	FILE NAPRALERT
1	FILE NIOSHTIC
2	FILE NTIS
31	FILE PAPERCHEM2
455	FILE PASCAL
93	FILE PROMT

```
          3   FILE RAPRA
        943   FILE SCISEARCH
          1   FILE USAN
          1   FILE WSCA

  33 FILES HAVE ONE OR MORE ANSWERS,   46 FILES SEARCHED IN STNINDEX

L2   QUE PROANTHOCYANIDIN

=> s l2 and (isolation or purification and grape or apple)
         33   FILE AGRICOLA
          9   FILE ANABSTR
         37   FILE BABS
         11   FILE BIOTECHNO
         56   FILE CABA
          1   FILE CAOLD
        245   FILE CAPLUS
          1   FILE CBNB
          6   FILE FEDRIP
  27 FILES SEARCHED...
         10   FILE IPA
         19   FILE JICST-EPLUS
          2   FILE KOSMET
        182   FILE NAPRALERT
          4   FILE PAPERCHEM2
         94   FILE PASCAL
          5   FILE PROMT
         95   FILE SCISEARCH

  17 FILES HAVE ONE OR MORE ANSWERS,   46 FILES SEARCHED IN STNINDEX

L3   QUE L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)

=> s l3 and ribosylation
          1   FILE CAPLUS
  27 FILES SEARCHED...

   1 FILES HAVE ONE OR MORE ANSWERS,   46 FILES SEARCHED IN STNINDEX

L4   QUE L3 AND RIBOSYLATION

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               7.42       7.63

FILE 'CAPLUS' ENTERED AT 14:42:58 ON 21 NOV 2002
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FILE COVERS 1907 - 21 Nov 2002 VOL 137 ISS 21
FILE LAST UPDATED: 20 Nov 2002 (20021120/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l4
          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
        212760 ISOLATION
           904 ISOLATIONS
        213341 ISOLATION
                 (ISOLATION OR ISOLATIONS)
        257701 PURIFICATION
           841 PURIFICATIONS
        258276 PURIFICATION
                 (PURIFICATION OR PURIFICATIONS)
        241149 PURIFN
           229 PURIFNS
        241251 PURIFN
                 (PURIFN OR PURIFNS)
        383827 PURIFICATION
                 (PURIFICATION OR PURIFN)
         20871 GRAPE
          9869 GRAPES
         24030 GRAPE
                 (GRAPE OR GRAPES)
         26928 APPLE
         11137 APPLES
         30175 APPLE
                 (APPLE OR APPLES)
          5305 RIBOSYLATION
            31 RIBOSYLATIONS
          5308 RIBOSYLATION
                 (RIBOSYLATION OR RIBOSYLATIONS)
L5           1 L3 AND RIBOSYLATION

=> dis l5 bib abs

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   2000:573663  CAPLUS
DN   133:155395
TI   ADP-ribosylation inhibitors and remedies for endotoxic bacterial
     enteric infection containing proanthocyanidin as the active
     ingredient
IN   Noda, Masatoshi; Kanda, Tomomasa; Yanagida, Akio; Hieda, Kazuo
PA   The Nikka Whisky Distilling Co., Ltd., Japan
SO   PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 2000047204      A1    20000817      WO 1999-JP648    19990215
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
             NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
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UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9924404 A1 20000829 AU 1999-24404 19990215
EP 1153604 A1 20011114 EP 1999-903920 19990215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI WO 1999-JP648 A 19990215

AB The invention relates to remedies for endotoxic bacterial enteric infection which contain as the active ingredient **proanthocyanidin** -contg. materials derived from natural matters such as **apple** ext. or grape ext. and inhibit and attenuate toxins produced by endotoxic bacteria causative of enteric infection typified by pathogenic vibrio (Vibrio cholerae, Vibrio parahaemolyticus), thus being efficacious in fundamentally treating and preventing the infection; medicinal compns. for treating/preventing diphtheria, etc. with the use of the ADP-**ribosylation** inhibitory effect of **proanthocyanidin**; food additives usable in preventing and treating the above diseases; and foods contg. these additives.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l2
1030 PROANTHOCYANIDIN
1914 PROANTHOCYANIDINS
L6 2046 PROANTHOCYANIDIN
(PROANTHOCYANIDIN OR PROANTHOCYANIDINS)

=> s l3
1030 PROANTHOCYANIDIN
1914 PROANTHOCYANIDINS
2046 PROANTHOCYANIDIN
(PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
212760 ISOLATION
904 ISOLATIONS
213341 ISOLATION
(ISOLATION OR ISOLATIONS)
257701 PURIFICATION
841 PURIFICATIONS
258276 PURIFICATION
(PURIFICATION OR PURIFICATIONS)
241149 PURIFN
229 PURIFNS
241251 PURIFN
(PURIFN OR PURIFNS)
383827 PURIFICATION
(PURIFICATION OR PURIFN)
20871 GRAPE
9869 GRAPES
24030 GRAPE
(GRAPE OR GRAPES)
26928 APPLE
11137 APPLES
30175 APPLE
(APPLE OR APPLES)
L7 245 L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)

=> s l7 and resin
494707 RESIN
334809 RESINS
610404 RESIN
(RESIN OR RESINS)

```
L8            8 L7 AND RESIN

=> s l8 and (styrene or anionic or octadecyl or octyl or silica)
         232977 STYRENE
           4062 STYRENES
         234139 STYRENE
                  (STYRENE OR STYRENES)
          95361 ANIONIC
            236 ANIONICS
          95456 ANIONIC
                  (ANIONIC OR ANIONICS)
          12546 OCTADECYL
              1 OCTADECYLS
          12547 OCTADECYL
                  (OCTADECYL OR OCTADECYLS)
          35460 OCTYL
              4 OCTYLS
          35463 OCTYL
                  (OCTYL OR OCTYLS)
         390172 SILICA
           2977 SILICAS
         390508 SILICA
                  (SILICA OR SILICAS)
L9            2 L8 AND (STYRENE OR ANIONIC OR OCTADECYL OR OCTYL OR SILICA)

=> dis l9 1-2 bib abs

L9   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2002 ACS
AN   1994:532679  CAPLUS
DN   121:132679
TI   Isolation of proanthocyanidins with polystyrene
     resins
IN   Horii, Shoji
PA   Hojo Seiansho Kk, Japan
SO   Jpn. Kokai Tokkyo Koho, 6 pp.
     CODEN: JKXXAF
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   JP 06049053        A2   19940222       JP 1992-202708   19920729
     JP 07062014        B4   19950705
AB   Proanthocyanidins, useful as antioxidants or discoloration
     inhibitors for foods or physiol. active substances (no data), are isolated
     from solns., such as bean-soaking or -boiling water in manuf. of bean jam,
     by adsorption on polystyrene adsorption resins, optional
     washing, drying, and elution with polar solvents with low polarity.
     Adzuki beans (10 kg) were soaked in H2O for .apprx.16 h, the soaking water
     was treated with Sepabeads sp 850 (adsorption resin) at room
     temp. for .apprx.2 h, dried at .ltoreq.70.degree., and eluted with 60%
     EtOH at 70.degree. for 2 h to give proanthocyanidins.

L9   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2002 ACS
AN   1983:469116  CAPLUS
DN   99:69116
TI   Application of high porous polymer to horticultural products.  I.
     Adsorption and elution of polyphenolic compounds
AU   Matsuo, Tomoaki; Takatsu, Tomoko; Itoo, Saburo
CS   Fac. Agric., Kagoshima Univ., Kagoshima, Japan
SO   Kagoshima Daigaku Nogakubu Gakujutsu Hokoku (1983), (33), 21-8
     CODEN: KADNAU; ISSN: 0453-0845
DT   Journal
LA   Japanese
```

AB Adsorption of polyphenols in horticultural products on poly(**styrene**-divinylbenzene) **resin** (Diaion HP-20) [55353-13-4], was examd. Highly polar compds. such as carbohydrates, amino acids, org. acids, bases and L-ascorbic acid were not adsorbed. (+)-Catechin [154-23-4], tannic acid, and naringin [10236-47-2] in aq. soln. were well adsorbed by this **resin**, while gallic acid and a polar phenol were not. The poolyphenols were eluted by 10-50% EtOH, with recoveries of 95-100%. Phenolic substances in hot water exts. of green and black tea were removed almost completely by the **resin**. When grape juice was passed through the **resin**, the initial fresh color was lost completely. The adsorbed pigments were recovered by eluting with 20-40% EtOH. No **apple** juice aroma was detected in an effluent from the column. All **proanthocyanidins** from young loquat fruit were adsorbed by this **resin**. TLC showed that **proanthocyanidins** of higher polymn. degrees were eluted as the EtOH concn. increased.

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=> s l2 and ribosylation
          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
          5305 RIBOSYLATION
            31 RIBOSYLATIONS
          5308 RIBOSYLATION
                 (RIBOSYLATION OR RIBOSYLATIONS)
L10          1 L2 AND RIBOSYLATION

=> s l10 and inhibit?
       1527099 INHIBIT?
L11          1 L10 AND INHIBIT?

=> dis l11 bib abs

L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   2000:573663  CAPLUS
DN   133:155395
TI   ADP-ribosylation inhibitors and remedies for endotoxic
     bacterial enteric infection containing proanthocyanidin as the
     active ingredient
IN   Noda, Masatoshi; Kanda, Tomomasa; Yanagida, Akio; Hieda, Kazuo
PA   The Nikka Whisky Distilling Co., Ltd., Japan
SO   PCT Int. Appl., 17 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
PI   WO 2000047204      A1   20000817       WO 1999-JP648     19990215
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
             NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
             UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9924404         A1   20000829       AU 1999-24404     19990215
     EP 1153604         A1   20011114       EP 1999-903920    19990215
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRAI WO 1999-JP648      A    19990215
```

AB The invention relates to remedies for endotoxic bacterial enteric infection which contain as the active ingredient **proanthocyanidin** -contg. materials derived from natural matters such as apple ext. or grape ext. and **inhibit** and attenuate toxins produced by endotoxic bacteria causative of enteric infection typified by pathogenic vibrio (Vibrio cholerae, Vibrio parahaemolyticus), thus being efficacious in fundamentally treating and preventing the infection; medicinal compns. for treating/preventing diphtheria, etc. with the use of the ADP-**ribosylation inhibitory** effect of **proanthocyanidin**; food additives usable in preventing and treating the above diseases; and foods contg. these additives.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s l2 and enterptox?
          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
             0 ENTERPTOX?
L12          0 L2 AND ENTERPTOX?

=> s l2 and enterotox?
          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
          8640 ENTEROTOX?
L13          0 L2 AND ENTEROTOX?

=> s l2 and (cholera or botulinus or traveler and diarrhea)
          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
         11196 CHOLERA
             2 CHOLERAS
         11197 CHOLERA
                 (CHOLERA OR CHOLERAS)
           286 BOTULINUS
           163 TRAVELER
           212 TRAVELERS
           330 TRAVELER
                 (TRAVELER OR TRAVELERS)
         12729 DIARRHEA
           107 DIARRHEAS
         12777 DIARRHEA
                 (DIARRHEA OR DIARRHEAS)
L14          4 L2 AND (CHOLERA OR BOTULINUS OR TRAVELER AND DIARRHEA)

=> dis l14 1-4 bib abs

L14  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:777747  CAPLUS
DN   137:284369
TI   Proteotoxin neutralizers containing proanthocyanidins from hop
IN   Tagashira, Motoyuki; Iwamaru, Yoshifumi; Noda, Masatoshi; Miyake, Masami
PA   Asahi Breweries, Ltd., Japan
SO   PCT Int. Appl., 29 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
```

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002078726	A1	20021010	WO 2002-JP3046	20020328
	W: AU, CN, JP, NZ, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
PRAI	JP 2001-92303	A	20010328		
	JP 2001-334722	A	20011031		

AB Disclosed are proteotoxin neutralizers contg. as the active ingredient **proanthocyanidins** obtained from hop. **Proanthocyanidins** were isolated from hop, and their inhibitory effects on ADP-ribosyltransferase activity of **cholera** toxin, and RNA N-glycosidase activity of vero toxin were examd.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:101948 CAPLUS
DN 134:352392
TI Studies on characteristics of polyphenols in apples
AU Kanda, Tomomasa
CS Nikka Whisky Distilling Co., Ltd., Sakaemachi, Hirosaki-shi, Aomori, 036-8336, Japan
SO Foods & Food Ingredients Journal of Japan (2001), 190, 15-22
CODEN: FFIJER; ISSN: 0919-9772
PB FFI Janaru
DT Journal; General Review
LA English

AB A review with 41 refs. Apples (Rosaceae Malus sp.) are recognized as the edible fruits that contribute to human health, represented by the proverb "an apple a day keeps the doctor away". It is well known that apples contain the simple polyphenols such as chlorogenic acid, (+)-catechin, (-)-epicatechin, phloridzin, rutin and other flavonoids, and **proanthocyanidins** such as procyanidin B1 and B2, that cause bitterness, astringency and browning of apple products. However, the functional and structural characteristics of all polyphenols in apples have not been analyzed. Total polyphenol content in thinned out immature apples was about ten times higher than in mature apples. Total crude apple polyphenol fraction was obtained from the juice of immature apples in the presence of sulfurous acid by reverse-phase column chromatog. Apple condensed tannin (CT) fraction was sepd. from the total polyphenol fraction by Sephadex LH-20, Toyopearl HW-40 or Diaion HP-20 column. CT was contained in catechins and **proanthocyanidins** (catechin oligomers), then the mol. size information for polymn. was obtained larger than pentadecamer using Matrix assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS). Reverse-phase high performance liq. chromatog., spectrophotometry and MALDI-TOF MS provided evidence that **proanthocyanidins** in apples were composed of procyanidins contg. no gallic acid esters. Physiol. functions of polyphenols in apples such as antioxidative, superoxide scavenging, cholesterol decreasing, hypotensive antiallergic, caries protective, deodorizing, desmutagenic and **cholera** toxin inhibiting activities were found in consecutive studies up to the present. Above all, it was suggested that antiallergic effects were based on the results, inhibition of hyaluronidase, inhibition of histamine release from RBL-2H3 cells and rat mast cells, inhibition of allergic reaction on the model mouse and decreasing of itch in atopic dermatitis. The method of high purity and large scale purifn. of procyanidin oligomers for industry use was developed. Normal-phase high performance liq. chromatog. of procyanidin oligomers made the sepn. in accordance with the d.p. catechin units.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1996:255341 CAPLUS
DN 124:337900
TI **Proanthocyanidin** polymers with antisecretory activity and **proanthocyanidin** oligomers from Guazuma ulmifolia bark
AU Hoer, Michaela; Heinrich, Michael; Rimpler, Horst
CS Inst. Pharmazeutische Biologie, Albert-Ludwigs-Univ., Freiburg, D-79104, Germany
SO Phytochemistry (1996), 42(1), 109-19
CODEN: PYTCAS; ISSN: 0031-9422
PB Elsevier
DT Journal
LA English
AB Bioassay-guided fractionation of a crude ext. of Guazuma ulmifolia bark led to the isolation of polymeric **proanthocyanidins** which inactivated **cholera** toxin (CT). The av. d.p. of the active compds. ranged from 14.4 to 32.0. The polymers consisted mainly of (-)-epicatechin units. In polymers of a representative fraction, the flavanol units were connected by [4.fwdarw.8] bonds and, less frequently, by [4.fwdarw.6] bonds. Inhibition of CT by tannins increased with Mr and conformation flexibility of the tannin mol. Several known procyanidin oligomers were also isolated. 1H NMR shift rules to distinguish between [4.fwdarw.8] and [4.fwdarw.6] linked **proanthocyanidin** peracetates, that have been proposed for dimers, were extended to trimers and a tetramer. A further diagnostic shift parameter to det. the interflavanoid bonding position is presented and the conformation of oligomeric **proanthocyanidin** peracetates is discussed.

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1995:732188 CAPLUS
DN 123:160543
TI Inhibition of intestinal chloride secretion by **proanthocyanidins** from Guazuma ulmifolia
AU Hoer, Michaela; Rimpler, Horst; Heinrich, Michael
CS Inst. Pharmazeutische Biologie, Albert-Ludwigs-Univ., Freiburg, D-79104, Germany
SO Planta Medica (1995), 61(3), 208-12
CODEN: PLMEAA; ISSN: 0032-0943
PB Thieme
DT Journal
LA English
AB The antisecretory activity of Guazuma ulmifolia bark was examd. in rabbit distal colon mounted in an Ussing chamber. Chloride secretion was stimulated by **cholera** toxin and prostaglandin E2 (PGE2). Guazuma ulmifolia ext. (GUE) completely inhibited **cholera** toxin-induced secretion if the ext. was added to the mucosal bath prior to the toxin. Adding the ext. after administration of the toxin had no effect on secretion. GUE did not inhibit PGE2-induced chloride secretion. These results indicate an indirect antisecretory mechanism. SDS-PAGE anal. of **cholera** toxin treated with GUE confirmed this presumption. GUE specifically interacted with the A subunit of the toxin. Preliminary phytochem. examns. showed that the most active fraction contains procyanidins with a d.p. higher than 8.

=> dis hist

(FILE 'HOME' ENTERED AT 14:34:15 ON 21 NOV 2002)

INDEX 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 14:34:43 ON 21 NOV 2002

```
                SEA PROANTHOCYANIDI
               ---------
L1              QUE PROANTHOCYANIDI
               ---------
                SEA PROANTHOCYANIDIN
               ---------
             398   FILE AGRICOLA
              68   FILE ANABSTR
               4   FILE APOLLIT
             223   FILE BABS
               1   FILE BIOCOMMERCE
             105   FILE BIOTECHNO
             671   FILE CABA
              11   FILE CAOLD
            2046   FILE CAPLUS
              11   FILE CBNB
              12   FILE CEABA-VTB
               2   FILE CEN
               4   FILE CIN
              17   FILE COMPENDEX
              20   FILE CONFSCI
               2   FILE ENCOMPLIT
               2   FILE ENCOMPLIT2
              17   FILE FEDRIP
               8   FILE GENBANK
               3   FILE INVESTEXT
              32   FILE IPA
              96   FILE JICST-EPLUS
               8   FILE KOSMET
             249   FILE NAPRALERT
               1   FILE NIOSHTIC
               2   FILE NTIS
              31   FILE PAPERCHEM2
             455   FILE PASCAL
              93   FILE PROMT
               3   FILE RAPRA
             943   FILE SCISEARCH
               1   FILE USAN
               1   FILE WSCA
L2              QUE PROANTHOCYANIDIN
               ---------
                SEA L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)
               ---------
              33   FILE AGRICOLA
               9   FILE ANABSTR
              37   FILE BABS
              11   FILE BIOTECHNO
              56   FILE CABA
               1   FILE CAOLD
             245   FILE CAPLUS
               1   FILE CBNB
               6   FILE FEDRIP
              10   FILE IPA
              19   FILE JICST-EPLUS
               2   FILE KOSMET
             182   FILE NAPRALERT
               4   FILE PAPERCHEM2
              94   FILE PASCAL
               5   FILE PROMT
              95   FILE SCISEARCH
L3              QUE L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)
               ---------
                SEA L3 AND RIBOSYLATION
               ---------
```

```
              1   FILE CAPLUS
L4             QUE L3 AND RIBOSYLATION
              ---------

     FILE 'CAPLUS' ENTERED AT 14:42:58 ON 21 NOV 2002
L5            1 S L4
L6         2046 S L2
L7          245 S L3
L8            8 S L7 AND RESIN
L9            2 S L8 AND (STYRENE OR ANIONIC OR OCTADECYL OR OCTYL OR SILICA)
L10           1 S L2 AND RIBOSYLATION
L11           1 S L10 AND INHIBIT?
L12           0 S L2 AND ENTERPTOX?
L13           0 S L2 AND ENTEROTOX?
L14           4 S L2 AND (CHOLERA OR BOTULINUS OR TRAVELER AND DIARRHEA)

=> index polymers
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    76.25      83.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.96      -4.96

INDEX 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, EMA, IFIPAT, JICST-EPLUS, PASCAL,
       PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH, USPATFULL, USPAT2, WPIDS,
       WPINDEX, WTEXTILES' ENTERED AT 14:56:47 ON 21 NOV 2002

20 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s proanthocyanidin
          4   FILE APOLLIT
        223   FILE BABS
       2046   FILE CAPLUS
         11   FILE CBNB
          2   FILE CEN
          4   FILE CIN
          1   FILE EMA
         83   FILE IFIPAT
         96   FILE JICST-EPLUS
        455   FILE PASCAL
         93   FILE PROMT
          3   FILE RAPRA
        943   FILE SCISEARCH
        202   FILE USPATFULL
          7   FILE USPAT2
        133   FILE WPIDS
  18 FILES SEARCHED...
        133   FILE WPINDEX

  17 FILES HAVE ONE OR MORE ANSWERS,   20 FILES SEARCHED IN STNINDEX

L15  QUE PROANTHOCYANIDIN

=> s l15 and ribosylation
          1   FILE CAPLUS
          1   FILE WPIDS
          1   FILE WPINDEX

   3 FILES HAVE ONE OR MORE ANSWERS,   20 FILES SEARCHED IN STNINDEX
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L16  QUE L15 AND RIBOSYLATION

=> file wpindex
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       1.59      85.47

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -4.96

FILE 'WPINDEX' ENTERED AT 14:58:22 ON 21 NOV 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

FILE LAST UPDATED:          20 NOV 2002      <20021120/UP>
MOST RECENT DERWENT UPDATE:     200275        <200275/DW>
 DERWENT WORLD PATENTS INDEX, COVERS 1963 TO DATE

 >>> STRUCTURE SEARCH WPINDEX USING DERWENT CHEMISTRY RESOURCE <<<

 >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

 >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
     SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

 >>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
     PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

 >>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
     GUIDES, PLEASE VISIT:
     http://www.derwent.com/userguides/dwpi_guide.html <<<

=> s l16
           102 PROANTHOCYANIDIN
            43 PROANTHOCYANIDINS
           133 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
            59 RIBOSYLATION
L17          1 L15 AND RIBOSYLATION

=> dis l17 bib abs

L17  ANSWER 1 OF 1  WPINDEX  (C) 2002 THOMSON DERWENT
AN   2000-549081 [50]   WPINDEX
DNC  C2000-163913
TI   Adenosine-5'-diphosphate-ribosylation inhibitors comprising
     proanthocyanidin containing material, useful for treating
     bacterial infections.
DC   B03 D13
IN   HIEDA, K; KANDA, T; NODA, M; YANAGIDA, A
PA   (NIKK-N) NIKKA WHISKY DISTILLING CO LTD; (NODA-I) NODA M; (MASA-I)
     MASATOSHI N; (NITK-N) NITKAU WHISKEY KK
CYC  82
PI   WO 2000047204 A1 20000817 (200050)* JA   17p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
            GH GM HR HU ID IL IS JP KE KG KR KZ LC LK LR LS LT LU LV MD MG MK
            MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US
            UZ VN YU ZW
     AU 9924404    A  20000829 (200062)
     EP 1153604    A1 20011114 (200175)  EN
```

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
KR 2001108193 A 20011207 (200236)
JP 2000598156 X 20020528 (200238)
CN 1348368 A 20020508 (200253)
ADT WO 2000047204 A1 WO 1999-JP648 19990215; AU 9924404 A AU 1999-24404 19990215, WO 1999-JP648 19990215; EP 1153604 A1 EP 1999-903920 19990215, WO 1999-JP648 19990215; KR 2001108193 A WO 1999-JP648 19990215, KR 2001-710070 20010809; JP 2000598156 X WO 1999-JP648 19990215, JP 2000-598156 19990215; CN 1348368 A CN 1999-816554 19990215, WO 1999-JP648 19990215
FDT AU 9924404 A Based on WO 200047204; EP 1153604 A1 Based on WO 200047204; JP 2000598156 X Based on WO 200047204
PRAI WO 1999-JP648 19990215
AN 2000-549081 [50] WPINDEX
AB WO 200047204 A UPAB: 20001010
NOVELTY - Adenosine-5'-diphosphate (ADP)-**ribosylation** inhibitors comprise **proanthocyanidin** containing material, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a composition for treating and preventing enteric infection caused by endotoxic bacteria comprising **proanthocyanidin** containing material.
ACTIVITY - Antimicrobial.
MECHANISM OF ACTION - Adenosine-Diphosphate-**Ribosylation** -inhibitor.
In assays, an apple extract at 25 mu g/ml containing 51% of **proanthocyanidin** B2 inhibited cholera toxin ADP-**ribosylation** by 95.4%
USE - As adenosine-5'-diphosphate-**ribosylation** inhibitors for treating and preventing enteric infection caused by endotoxic bacteria (e.g. Vibrio cholerae and Vibrio parahaemolyticus) such as cholera, botulism and diseases picked up whilst travelling, as well as whooping cough, tetanus and opportunistic infections.
Dwg.0/1

```
=> s l15 and (isolation or purification)
           102 PROANTHOCYANIDIN
            43 PROANTHOCYANIDINS
           133 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
         49280 ISOLATION
           175 ISOLATIONS
         49366 ISOLATION
                 (ISOLATION OR ISOLATIONS)
         80067 PURIFICATION
           152 PURIFICATIONS
         80154 PURIFICATION
                 (PURIFICATION OR PURIFICATIONS)
         34099 PURIFICN
            42 PURIFICNS
         34125 PURIFICN
                 (PURIFICN OR PURIFICNS)
           948 PURIFN
             2 PURIFNS
           949 PURIFN
                 (PURIFN OR PURIFNS)
         92912 PURIFICATION
                 (PURIFICATION OR PURIFICN OR PURIFN)
L18         8 L15 AND (ISOLATION OR PURIFICATION)

=> index
ENTER FILE OR CLUSTER NAMES (NONE):end

=> index polymers
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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                       13.36      98.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                          ENTRY    SESSION
CA SUBSCRIBER PRICE                                        0.00      -4.96

INDEX 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, EMA, IFIPAT, JICST-EPLUS, PASCAL,
       PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH, USPATFULL, USPAT2, WPIDS,
       WPINDEX, WTEXTILES' ENTERED AT 15:00:19 ON 21 NOV 2002

20 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s l15 and (purification or isolation)
         41   FILE BABS
        191   FILE CAPLUS
          4   FILE IFIPAT
         16   FILE JICST-EPLUS
         95   FILE PASCAL
          7   FILE PROMT
         69   FILE SCISEARCH
         76   FILE USPATFULL
          1   FILE USPAT2
          8   FILE WPIDS
          8   FILE WPINDEX

  11 FILES HAVE ONE OR MORE ANSWERS,    20 FILES SEARCHED IN STNINDEX

L19  QUE L15 AND (PURIFICATION OR ISOLATION)

=> s l19 and (resin and styrene or anionic or octyl or octadecyl or phenyl)
          3   FILE CAPLUS
          1   FILE PROMT
  15 FILES SEARCHED...
         24   FILE USPATFULL
          1   FILE USPAT2
          2   FILE WPIDS
          2   FILE WPINDEX

   6 FILES HAVE ONE OR MORE ANSWERS,    20 FILES SEARCHED IN STNINDEX

L20  QUE L19 AND (RESIN AND STYRENE OR ANIONIC OR OCTYL OR OCTADECYL OR PHENYL)


=> file uspatfull
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY    SESSION
FULL ESTIMATED COST                                        3.71     102.54

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                          ENTRY    SESSION
CA SUBSCRIBER PRICE                                        0.00      -4.96

FILE 'USPATFULL' ENTERED AT 15:04:13 ON 21 NOV 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Nov 2002 (20021121/PD)
FILE LAST UPDATED: 21 Nov 2002 (20021121/ED)
HIGHEST GRANTED PATENT NUMBER: US6484318
HIGHEST APPLICATION PUBLICATION NUMBER: US2002174474
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CA INDEXING IS CURRENT THROUGH 21 Nov 2002 (20021121/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Nov 2002 (20021121/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2002

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l20
L20 110 PROANTHOCYANIDIN
L20 158 PROANTHOCYANIDINS
L20 202 PROANTHOCYANIDIN
(PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
L21 148840 PURIFICATION
L21 2963 PURIFICATIONS
L21 149306 PURIFICATION
(PURIFICATION OR PURIFICATIONS)
L22 186398 ISOLATION
L22 2001 ISOLATIONS
L22 186691 ISOLATION
(ISOLATION OR ISOLATIONS)
L23 376441 RESIN
L23 190451 RESINS
L23 422480 RESIN
(RESIN OR RESINS)
L24 133947 STYRENE
L24 10361 STYRENES
L24 135110 STYRENE
(STYRENE OR STYRENES)
L25 83496 ANIONIC
L25 1315 ANIONICS
L25 83639 ANIONIC
(ANIONIC OR ANIONICS)
L26 68347 OCTYL
L26 271 OCTYLS
L26 68477 OCTYL
(OCTYL OR OCTYLS)
L27 23882 OCTADECYL
L27 23 OCTADECYLS
L27 23902 OCTADECYL
(OCTADECYL OR OCTADECYLS)
L28 202565 PHENYL
L28 1254 PHENYLS
L28 202707 PHENYL

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                (PHENYL OR PHENYLS)
L21         24 L19 AND (RESIN AND STYRENE OR ANIONIC OR OCTYL OR OCTADECYL OR
               PHENYL)

=> s l21 and (water or alcohol or ester or ketone)
        977502 WATER
         31113 WATERS
        979550 WATER
                 (WATER OR WATERS)
        315633 ALCOHOL
        184484 ALCOHOLS
        361469 ALCOHOL
                 (ALCOHOL OR ALCOHOLS)
        230733 ESTER
        223045 ESTERS
        306635 ESTER
                 (ESTER OR ESTERS)
        115380 KETONE
         75729 KETONES
        143041 KETONE
                 (KETONE OR KETONES)
L22         24 L21 AND (WATER OR ALCOHOL OR ESTER OR KETONE)

=> dis l22 1-24 bib abs

L22  ANSWER 1 OF 24  USPATFULL
AN     2002:307539  USPATFULL
TI     Hair-growing agent
IN     Kamimura, Ayako, Tsukuba-shi, JAPAN
       Takahashi, Tomoya, Tsuchiura-shi, JAPAN
       Mimura, Takashi, Shinagawa-ku, JAPAN
       Honda, Shinkichi, Nagareyama-shi, JAPAN
PA     Kyowa Hakko Kogyo Co., Ltd., Chiyoda-ku, JAPAN (non-U.S. corporation)
PI     US 2002172657      A1   20021121
AI     US 2002-73113      A1   20020212 (10)
PRAI   JP 2001-40351       20010216
DT     Utility
FS     APPLICATION
LREP   FITZPATRICK CELLA HARPER & SCINTO, 30 ROCKEFELLER PLAZA, NEW YORK, NY,
       10112
CLMN   Number of Claims: 21
ECL    Exemplary Claim: 1
DRWN   No Drawings
LN.CNT 920
AB     The present invention provides a hair-growing agent comprising, as an
       active ingredient, a phosphatidic acid represented by formula (I):
       ##STR1##

       (wherein R.sup.1 represents alkyl, alkenyl, alkanoyl or alkenoyl; and
       when R.sup.1 represents alkyl or alkenyl, R.sup.2 represents alkyl,
       alkenyl, alkanoyl or alkenoyl, and when R.sup.1 represents alkanoyl or
       alkenoyl, R.sup.2 represents alkyl or alkenyl).


L22  ANSWER 2 OF 24  USPATFULL
AN     2002:304078  USPATFULL
TI     Method of isolating mucilaginous polysaccharides and uses thereof
IN     Vittori, Natale, Coppell, TX, United States
PA     Biotechnology Services and Consulting, Inc., Coppell, TX, United States
       (U.S. corporation)
PI     US 6482942         B1   20021119
AI     US 2000-481111          20000111 (9)
PRAI   US 1999-115619P     19990112 (60)
DT     Utility
```

FS GRANTED
EXNAM Primary Examiner: Wilson, James O.; Assistant Examiner: Maier, Leigh C.
LREP Akin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1367
AB The present invention provides a method of isolating mucilaginous polysaccharides from plants, cereals, cell cultures, or fungi such as mushrooms known to have mucilaginous or protein-bound polysaccharides with desirable biological properties. The mucilaginous polysaccharides present in aqueous solution or tissue extracts are treated with tannins to form a complex which is then separated from the solution. The complex is then treated one or more times with either solvents or other substances in solution to remove the bounded tannins from the complex thereby and releasing the isolated polysaccharide. The polysaccharides prepared according to the present method retain properties that are substantially similar to those of the native polysaccharide as it is found in the respective plant or cell. The polysaccharides thus prepared are used in a variety of products. This process is particularly suitable for isolating acetylated mannose polymers from aloe plants and beta glucans.

L22 ANSWER 3 OF 24 USPATFULL
AN 2002:294342 USPATFULL
TI Aquatic animal treatment method and composition containing pimenta extract
IN Yoshpa, Michael, Doylestown, PA, UNITED STATES
PA Aquarium Pharmaceuticals, Inc., Chalfont, PA, UNITED STATES (U.S. corporation)
PI US 2002164384 A1 20021107
AI US 2001-797744 A1 20010302 (9)
DT Utility
FS APPLICATION
LREP AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P., ONE COMMERCE SQUARE, 2005 MARKET STREET, SUITE 2200, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 756
AB A therapeutic method for treating diseased or injured fish or other aquatic animal includes administering to the fish or other aquatic animal an amount of Pimenta extract selected from the group consisting of Pimenta racemosa and Pimenta dioica sufficient to promote recovery of the diseased or injured fish or other aquatic animal. Also disclosed is a prophylactic method for treating a disease-free fish or other aquatic animal, including adding to **water** containing or to contain the fish or other aquatic animal Pimenta extract selected from the group consisting of Pimenta racemosa and Pimenta dioica in an amount effective to promote resistance of the aquatic animal to disease. An aqueous emulsion containing Pimenta extract oil in **water**, where the Pimenta extract is selected from the group consisting of Pimenta racemosa and Pimenta dioica is also disclosed for use in these methods.

L22 ANSWER 4 OF 24 USPATFULL
AN 2002:291095 USPATFULL
TI Synthesis of 4.alpha.-arylepicatechins
IN Kozikowski, Alan P., Princeton, NJ, United States
Romanczyk, Jr., Leo J., Hackettstown, NJ, United States
Tuckmantel, Werner, Washington, DC, United States
PA Mars Incorporated, Mclean, VA, United States (U.S. corporation)
PI US 6476241 B1 20021105

AI US 2000-655360 20000905 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Solola, T. A.
LREP Kelley, Margaret B., Clifford Chance US, LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1206
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Oligomeric procyanidins containing 4.alpha.-linked epicatechin units are rare in nature and have hitherto not been accessible through stereoselective synthesis. Provided herein is the preparation of the prototypical dimer, epicatechin-4.alpha.,8-epicatechin, by reaction of the protected 4-**ketones** with aryllithium reagents derived by halogen/metal exchange from the aryl bromides. Removal of the 4-hydroxyl group from the resulting tertiary benzylic **alcohols** is effected by tri-n-butyltin hydride and trifluoroacetic acid in a completely stereoselective manner, resulting in hydride delivery exclusively from the .beta. face.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 5 OF 24 USPATFULL
AN 2002:279745 USPATFULL
TI Process for extracting compounds from plants
IN Krasutsky, Pavel A., Duluth, MN, UNITED STATES
Nesterenko, Vitaliy V., Duluth, MN, UNITED STATES
PI US 2002155177 A1 20021024
AI US 2002-53237 A1 20020117 (10)
RLI Continuation-in-part of Ser. No. US 2001-969130, filed on 1 Oct 2001, PENDING
PRAI US 2000-236579P 20000929 (60)
DT Utility
FS APPLICATION
LREP SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A., P.O. BOX 2938, MINNEAPOLIS, MN, 55402
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 1603
AB The present invention provides a method for selectively extracting acidic and/or non-acidic compounds from natural material such as plant tissue.

L22 ANSWER 6 OF 24 USPATFULL
AN 2002:279654 USPATFULL
TI Hair-growing agent
IN Kamimura, Ayako, Tsukuba-shi, JAPAN
Takahashi, Tomoya, Tsuchiura-shi, JAPAN
Mimura, Takashi, Shinagawa-ku, JAPAN
Honda, Shinkichi, Nagareyama-shi, JAPAN
PA Kyowa Hakko Kogyo Co., Ltd., Chiyoda-ku, JAPAN (non-U.S. corporation)
PI US 2002155085 A1 20021024
AI US 2002-73107 A1 20020212 (10)
PRAI JP 2001-40350 20010216
DT Utility
FS APPLICATION
LREP FITZPATRICK CELLA HARPER & SCINTO, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 755
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a hair-growing agent comprising, as an active ingredient, a phosphatidic acid represented by formula (I): ##STR1##

(wherein R.sup.1 represents straight-chain alkyl having an odd number of carbon atoms, straight-chain alkenyl having an odd number of carbon atoms, or straight-chain alkynyl having an odd number of carbon atoms).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 7 OF 24 USPATFULL
AN 2002:243654 USPATFULL
TI Compositions and methods for the prevention and treatment of tissue ischemia
IN Miller, Guy Michael, San Jose, CA, UNITED STATES
Brown, Lesley A., San Jose, CA, UNITED STATES
Del Balzo, Ughetta, Morgan Hill, CA, UNITED STATES
Flaim, Stephen, San Diego, CA, UNITED STATES
Boddupalli, Sekhar, San Jose, CA, UNITED STATES
Wang, Bing, Cupertino, CA, UNITED STATES
PI US 2002132845 A1 20020919
AI US 2001-17717 A1 20011214 (10)
PRAI US 2000-256269P 20001215 (60)
US 2001-296581P 20010606 (60)
US 2001-296580P 20010606 (60)
US 2001-343575P 20011019 (60)
DT Utility
FS APPLICATION
LREP Gladys H. Monroy, Morrison & Foerster LLP, 755 Page Mill Road, Palo Alto, CA, 94304-1018
CLMN Number of Claims: 97
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 3908
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions and methods for the treatment of tissue ischemia, and in particular, cerebral ischemia. In particular, the present invention provides gamma-, beta-, or delta-tocopherol enriched tocopherol compositions and gamma-, beta-, or delta-tocopherol metabolite enriched compositions and/or flavonoid enriched and/or a flavonoid derivative enriched compositions and methods for their use in preventing or treating a tissue ischemic condition or a cerebral ischemic condition. The present invention also provides pharmaceutical compositions comprising gamma-, beta-, or delta-tocopherol enriched tocopherol composition, a gamma-, beta-, or delta-tocopherol metabolite enriched compositions or flavonoid enriched compositions or flavonoid derivative enriched compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 8 OF 24 USPATFULL
AN 2002:236289 USPATFULL
TI Synthetic methods for polyphenols
IN Romanczyk, Leo J., JR., Hackettstown, NJ, UNITED STATES
Kozikowski, Alan P., Princeton, NJ, UNITED STATES
Tueckmantel, Werner, Washington, DC, UNITED STATES
Lippman, Marc E., Bethesda, MD, UNITED STATES
PA Mars, Incorporated (U.S. corporation)
PI US 2002128493 A1 20020912
AI US 2001-17812 A1 20011214 (10)
RLI Continuation of Ser. No. US 1998-169554, filed on 9 Oct 1998, PENDING
Continuation-in-part of Ser. No. US 1997-948226, filed on 9 Oct 1997,

GRANTED, Pat. No. US 6207842
DT Utility
FS APPLICATION
LREP Margaret B. Kelley, Clifford Chance Rogers & Wells LLP, 200 Park Avenue, New York, NY, 10166-0153
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process is disclosed for the production of polyphenol oligomers having n polyphenol monomeric units, n being an integer from 2-18. The process includes coupling of a protected polyphenol, having protected phenolic hydroxyl groups, with a C-4 functionalized polyphenol monomer. The protected polyphenol may be a protected polyphenol monomer or a protected polyphenol oligomer having 2-17 monomeric units. Advantageously, polyphenol monomeric units forming the polyphenol oligomers may be the same or different flavanoid compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 9 OF 24 USPATFULL
AN 2002:213480 USPATFULL
TI Process for extracting compounds from plants
IN Krasutsky, Pavel A., Duluth, MN, UNITED STATES
Nesterenko, Vitaliy V., Rantoul, IL, UNITED STATES
PI US 2002114853 A1 20020822
AI US 2001-969130 A1 20011001 (9)
PRAI US 2000-236579P 20000929 (60)
DT Utility
FS APPLICATION
LREP SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A., P.O. BOX 2938, MINNEAPOLIS, MN, 55402
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 1455
AB The present invention provides a method for selectively extracting acidic and/or non-acidic compounds from natural material such as plant tissue.

L22 ANSWER 10 OF 24 USPATFULL
AN 2002:188360 USPATFULL
TI Formulations of tocopherols and methods of making and using them
IN Miller, Guy, Mountain View, CA, United States
Brown, Lesley A., Cupertino, CA, United States
PA Galileo Laboratories, Inc., Santa Clara, CA, United States (U.S. corporation)
PI US 6426362 B1 20020730
AI US 2000-684588 20001006 (9)
PRAI US 1999-158234P 19991008 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh; Assistant Examiner: Kwon, Brian-Yong
LREP Morrison & Foerster LLP
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3175
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Non-naturally-occuring compositions for use in amelioration of disruption of energy metabolism secondary to stress are described. The compositions comprise a tocopherol and/or a derivative thereof, and a

synergist, and are particularly suited for use as nutritional supplements. Synergists include, but are not limited to, flavonoids and lactoferrin and/or derivatives thereof. Compositions comprising an optimized formulation comprising a tocopherol and an additional compound such as daidzein or biochanin A are also described. Methods of making these compositions and methods of ameliorating injury(ies) or disruption of energy metabolism secondary to stress, comprising administering such compositions, are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 11 OF 24 USPATFULL
AN 2002:175317 USPATFULL
TI Synthetic methods for preparation of protected **proanthocyanidin** (s)
IN Romanczyk, Jr., Leo J., Hackettstown, NJ, United States
Kozikowski, Alan P., Princeton, NJ, United States
Tueckmantel, Werner, Washington, DC, United States
Lippman, Marc E., Bethesda, MD, United States
PA Mars, Incorporated, McLean, VA, United States (U.S. corporation)
PI US 6420572 B1 20020716
AI US 1998-169554 19981009 (9)
RLI Continuation-in-part of Ser. No. US 1997-948226, filed on 9 Oct 1997, now patented, Pat. No. US 6207842
DT Utility
FS GRANTED
EXNAM Primary Examiner: Henderson, C
LREP Kelley, Esq., Margaret B., Clifford Chance Rogers & Wells, LLP
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2263
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process is disclosed for the production of polyphenol oligomers having n polyphenol monomeric units, n being an integer from 2-18. The process includes coupling of a protected polyphenol, having protected phenolic hydroxyl groups, with a C-4 functionalized polyphenol monomer. The protected polyphenol may be a protected polyphenol monomer or a protected polyphenol oligomer having 2-17 monomeric units. Advantageously, polyphenol monomeric units forming the polyphenol oligomers may be the same or different flavanoid compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 12 OF 24 USPATFULL
AN 2002:48069 USPATFULL
TI Plant **proanthocyanidin** extracts
IN Walker, Edward B., Ogden, UT, UNITED STATES
Mickelsen, Richard A., Ogden, UT, UNITED STATES
Mickelsen, Jennifer N., Ogden, UT, UNITED STATES
PI US 2002028260 A1 20020307
AI US 2001-920511 A1 20010801 (9)
RLI Division of Ser. No. US 2001-822710, filed on 30 Mar 2001, PENDING
Division of Ser. No. US 1999-391308, filed on 7 Sep 1999, GRANTED, Pat. No. US 6210681
DT Utility
FS APPLICATION
LREP TRASK BRITT, P.O. BOX 2550, SALT LAKE CITY, UT, 84110
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 1280
AB Compounds isolated from plant materials, particularly plants of the genus Vaccinium, which have biological activity measurable as inhibition

with adhesion of bacterial cells to surfaces, and an extract of such plant materials which is significantly enriched for the anti-adhesion activity. The specific compounds include procyanidins (also known as "condensed tannins"), leukocyanin, leucodelphinin, flavonol glucosides including myricetin-3-pyranoside and **proanthocyanidin** extracts. These **proanthocyanidin** extracts are capable of inhibiting agglutination reactions of P-type E. Coli. The extracts containing **proanthocyanidins** contain at least one A-type interflavanoid bond. Methods of making an extract. Methods of preventing or treating urogenital infections in a mammal by administering a **proanthocyanidin** composition including the **proanthocyanidin** extract, a **proanthocyanidin** compound, a **proanthocyanidin** polymer or a mixture thereof, to a subjecct in an amount and for a time sufficient to prevent, reduce or eliminate symptoms associated with such infections.

L22 ANSWER 13 OF 24 USPATFULL
AN 2002:29401 USPATFULL
TI N-substituted amino acids, antioxidant pharmaceutical compositions containing n-substituted amino acids and methods for preventing cardiovascular diseases and/or preventing and/or treating antioxidant responsive diseases therewith
IN Tzodikov, Nathan, Haverford, PA, United States
PA Checkpoint, Genetics, Inc., Exton, PA, United States (U.S. corporation)
PI US 6346547 B1 20020212
AI US 2000-500064 20000208 (9)
PRAI US 1999-119030P 19990208 (60)
US 1999-167069P 19991123 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Russell, Jeffrey E.
LREP Venable, Gollin, Michael A., Haddaway, Keith G.
CLMN Number of Claims: 34
ECL Exemplary Claim: 14
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1452
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Low-toxicity, highly-bioavailable, pharmaceutical antioxidant compositions for preferred oral administration to mammals are provided which have at least one amino acid-based compound of the general formula (I):

A--N(Z)--CH(R.sup.1)C(O)--Q (I)

wherein A is represented by the formula:

XO--[C(R.sup.2).sub.2].sub.n--

wherein n is an integer of from 1 to about 3, X is selected from the group consisting of a hydrogen atom, an acyl group and a halogenated acyl group and each R.sup.2 is independently selected from the group consisting of a hydrogen atom, an alkyl group having from 1 to about 3 carbon atoms, a hydroxyalkyl group having from 1 to about 3 carbon atoms, and CH.sub.2OX; Z is selected from the group consisting of a hydrogen atom, an alkyl group of from 1 to about 3 carbon atoms, and A; R.sup.1 is an amino acid side chain group or an amino acid side chain group which forms with R.sup.2 a single heterocyclic structure having a total of from 5 to 7 atoms in the ring; and wherein Q is a substituent selected from the group consisting of a hydroxyl, --N(R.sup.2).sub.2, --NR.sup.2(NR.sup.2).sub.2, --SR.sup.2, an alkoxy, a halogenated alkoxy, an O-acyl and an O-halogenated acyl are disclosed. Methods of treating, delaying the onset of and/or preventing antioxidant responsive diseases comprising administering such pharmaceutical antioxidant compositions

and amino acid-based compounds of the general formula (I) are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 14 OF 24 USPATFULL
AN 2002:3677 USPATFULL
TI Method of altering and improving taste characteristics of edible consumables with monomeric or oligomeric polyphenolic compounds
IN Norris, Leslie Marie, Riverbank, CA, UNITED STATES
McCord, Jeffrey Dodd, San Raphael, CA, UNITED STATES
Henis, Jay M.S., St, Louis, MO, UNITED STATES
Hoehn, Matthias J., Roedental, GERMANY, FEDERAL REPUBLIC OF
PI US 2002001651 A1 20020103
AI US 2001-767123 A1 20010122 (9)
PRAI US 2000-178523P 20000124 (60)
DT Utility
FS APPLICATION
LREP Nestor W. Shust, 4616 Granger Road, Fairlawn, OH, 44333
CLMN Number of Claims: 77
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 1454
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is directed to a method of modifying or altering the taste and/or flavor characteristics, such as aromatics, blendedness, creaminess, mouthfeel, fullness, saltiness, sourness, bitterness, onset of initial flavor perception or **alcohol** perception, of edible consumables, especially brown foods, dairy products, citrus, alcoholic beverages, dietetic foods, low fat foods and fat-free foods, by incorporating in such foods or beverages an effective amount of a polyphenolic material selected from (a) a monomeric polyphenol, (b) an oligomeric polyphenol, (c) a mixture of monomeric and oligomeric polyphenolic materials and (d) a mixture of any or all of said polyphenolic materials with a polymeric polyphenolic material.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 15 OF 24 USPATFULL
AN 2001:202646 USPATFULL
TI Ophthalmic uses of PPARgamma agonists and PPARgamma antagonists
IN Pershadsingh, Harrihar A., Bakersfield, CA, United States
Levy, Daniel E., San Carlos, CA, United States
PA Photogenesis, Inc., Los Angeles, CA, United States (U.S. corporation)
PI US 6316465 B1 20011113
AI US 1999-342381 19990628 (9)
PRAI US 1998-90937P 19980627 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Dees, Jose' G.; Assistant Examiner: Williamson, Michael A.
LREP Brinks, Hofer, Gilson & Lione
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1661
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treating diseases of ocular tissues expressing the nuclear receptor PPAR.gamma., by inhibiting the inflammatory response, the neovascularization and angiogenesis, and programmed cell death (apoptosis) in these target tissues, comprising administering to a human or animal in need of treatment an effective amount of a compound that modifies the activity of PPAR.gamma., or pharmaceutically acceptable salts and solvates thereof.

Novel compounds and methods for their synthesis are provided, including a compound having the general structure: ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 16 OF 24 USPATFULL
AN 2001:193974 USPATFULL
TI **Proanthocyanidin**-containing composition
IN Takahasi, Tomoya, Ibaraki, Japan
Kabayashi, Asako, Ibaraki, Japan
PI US 2001036487 A1 20011101
AI US 2001-811594 A1 20010320 (9)
PRAI JP 2000-83647 20000324
DT Utility
FS APPLICATION
LREP FITZPATRICK CELLA HARPER & SCINTO, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 830
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A composition and method for stabilizing **proanthocyanidin**, especially for preventing, for example, its discoloration by oxidative polymerization. The method utilizes (and the composition contains) **proanthocyanidin**, and an amino acid having a hydroxyl group or a dipeptide containing said amino acid. Also shown is a drink, food, cosmetic or medicament which contains the composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 17 OF 24 USPATFULL
AN 2001:162864 USPATFULL
TI Antiobestic agent containing procyanidin as the active ingredient
IN Nakahara, Koichi, Osaka, Japan
Nakai, Masaaki, Osaka, Japan
Tamura, Yukiyoshi, Hiroshima-ken, Japan
PA Suntory Limited, Japan (non-U.S. corporation)
PI US 6294190 B1 20010925
WO 9723210 19970703
AI US 1997-894625 19970822 (8)
WO 1996-JP3810 19961226
19970822 PCT 371 date
19970822 PCT 102(e) date
PRAI JP 1995-338493 19951226
DT Utility
FS GRANTED
EXNAM Primary Examiner: Dodson, Shelley A.
LREP Manelli Denison & Selter, White, Jr., Paul E.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1162
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An antiobestic agent of the present invention having antiobestic effect, carbohydrase inhibitory effect, blood sugar increase inhibitory effect, monosaccharide absorption inhibitory effect, cholic acid adsorptive excretion promoting effect, cholesterol lowering effect, blood triglyceride lowering effect and lipase inhibitory effect and being useful not only as an antiobestic agent but also as an antilipotrophic agent, an antihyperlipemic agent, an antiarteriosclerotic agent and an antidiabetic agent. Tamarind seed coat extract containing a large amount of procyanidin, which is a trimer represented by the following formula

and serves as the active ingredient in the present invention, exhibits a potent antiobestic effect as such without the need for further **purification**. The antiobestic agent of the present invention is usable as a carbohydrase inhibitor, a blood sugar increase inhibitor, a monosaccharide absorption inhibitor, a cholic acid adsorptive excretion promoter, a cholesterol lowering agent, a blood triglyceride lowering agent and a lipase inhibitor. Moreover, use of the antiobestic agent makes it possible to produce foods or beverages and animal feeds having these effects, thus contributing to the relief or prevention of diabetes and obesity in our daily life ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 18 OF 24 USPATFULL
AN 2001:155467 USPATFULL
TI Plant **proanthocyanidin** extracts
IN Walker, Edward B., Ogden, UT, United States
Mickelsen, Richard A., JR., Ogden, UT, United States
Mickelsen, Jennifer N., Ogden, UT, United States
PI US 2001021398 A1 20010913
US 6440471 B2 20020827
AI US 2001-822710 A1 20010330 (9)
RLI Division of Ser. No. US 1999-391308, filed on 7 Sep 1999, GRANTED, Pat. No. US 6210681
DT Utility
FS APPLICATION
LREP TRASK BRITT, P.O. BOX 2550, SALT LAKE CITY, UT, 84110
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 1278
AB Compounds isolated from plant materials, particularly plants of the genus Vaccinium, which have biological activity measurable as inhibition with adhesion of bacterial cells to surfaces, and an extract of such plant materials which is significantly enriched for the anti-adhesion activity. The specific compounds include procyanidins (also known as "condensed tannins"), leukocyanin, leucodelphinin, flavonol glucosides including myricetin-3-pyranoside and **proanthocyanidin** extracts. These **proanthocyanidin** extracts are capable of inhibiting agglutination reactions of P-type E. coli. The extracts containing **proanthocyanidins** contain at least one A-type interflavanoid bond. Methods of making an extract. Methods of preventing or treating urogenital infections in a mammal by administering a **proanthocyanidin** composition including the **proanthocyanidin** extract, a **proanthocyanidin** compound, a **proanthocyanidin** polymer or a mixture thereof, to a subject in an amount and for a time sufficient to prevent, reduce or eliminate symptoms associated with such infections.

L22 ANSWER 19 OF 24 USPATFULL
AN 2001:47556 USPATFULL
TI Plant **proanthocyanidin** extracts
IN Walker, Edward B., Ogden, UT, United States
Mickelsen, Jr., Richard A., Ogden, UT, United States
Mickelsen, Jennifer N., Ogden, UT, United States
PA JLB, Inc., Ogden, UT, United States (U.S. corporation)
PI US 6210681 B1 20010403
AI US 1999-391308 19990907 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Weber, Jon P.; Assistant Examiner: Patten, Patricia D.
LREP Trask Britt
CLMN Number of Claims: 11

ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 764
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds isolated from plant materials, particularly plants of the genus Vaccinium, which have biological activity measurable as inhibition with adhesion of bacterial cells to surfaces, and an extract of such plant materials which is significantly enriched for the anti-adhesion activity. The specific compounds include procyanidins (also known as "condensed tannins"), leukocyanin and leucodelphinin, and flavonol glucosides including myricetin-3-pyranoside and **proanthocyanidin** extracts. These **proanthocyanidin** extracts are capable of inhibiting agglutination reactions of P-type E. coli. The extracts containing **proanthocyanidins** contain at least one A-type interflavanoid bond. Methods of making an extract having the properties. Methods of preventing or treating urogenital infections in a mammal by administering a **proanthocyanidin** composition including the **proanthocyanidin** extract, a **proanthocyanidin** compound, a **proanthocyanidin** polymer or a mixture thereof, to the mammal in an amount and for a time sufficient to prevent, reduce or eliminate the symptoms associated with such infections and thereby lead to an amelioration or curing of the infection.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 20 OF 24 USPATFULL
AN 2001:44399 USPATFULL
TI Process for preparing procyanidin(4-6 or 4-8) oligomers and their derivatives
IN Romanczyk, Jr., Leo J., Hackettstown, NJ, United States
Kozikowski, Alan P., Princeton, NJ, United States
Tueckmantel, Werner, Washington, DC, United States
PA Mars Incorporated, McLean, VA, United States (U.S. corporation)
PI US 6207842 B1 20010327
AI US 1997-948226 19971009 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Henderson, Christopher
LREP Kelley, Margaret B.Clifford Chance Rogers & Wells, LLP
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1668
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process is disclosed for the production of polyphenol oligomers having n polyphenol monomers, n being an integer from 2-18. The process includes coupling of a protected polyphenol, having protected phenolic hydroxyl groups, with a C-4 functionalized polyphenol monomer. The protected polyphenol may be a protected polyphenol monomer or a protected polyphenol oligomer having 2-17 monomers. Advantageously, polyphenol monomers forming the polyphenol oligomers may be the same or different.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 21 OF 24 USPATFULL
AN 2000:171019 USPATFULL
TI Preparation of fagopyritols and uses therefor
IN Obendorf, Ralph L., Ithaca, NY, United States
Horbowicz, Marcin, Prusa, Poland
PA Cornell Research Foundation, Inc., Ithaca, NY, United States (U.S. corporation)
PI US 6162795 20001219
AI US 1998-73467 19980506 (9)

PRAI US 1997-45927P 19970507 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Howard C.
LREP Nixon Peabody LLP
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 37 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 2421
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes isolated Fagopyritol A1, isolated Fagopyritol A2, and isolated Fagopyritol B3. Compositions which include two or more of Fagopyritol A1, Fagopyritol A2, Fagopyritol B1, Fagopyritol B2, Fagopyritol B3, and D-chiro-inositol, at least one of which is an isolated Fagopyritol A1, isolated Fagopyritol A2, or isolated Fagopyritol B3, are also disclosed. Methods for preparing substantially pure Fagopyritol A1, Fagopyritol A2, Fagopyritol B1, Fagopyritol B2, Fagopyritol B3, or mixtures thereof from buckwheat are also described. The fagopyritols can be used to prepare pharmaceutical compositions, the administration of which can be used to treat diabetes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 22 OF 24 USPATFULL
AN 2000:131414 USPATFULL
TI Hair-growing agent comprised of **proanthocyanidins**
IN Takahashi, Tomoya, Tsuchiura, Japan
Kobayashi, Yoshinori, Tsukuba, Japan
Kawamura, Michio, Hofu, Japan
Yokoo, Yoshiharu, Ushiku, Japan
Kamiya, Toshikazu, Machida, Japan
Tamaoki, Tatsuya, Machida, Japan
PA Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6126940 20001003
WO 9600561 19960111
AI US 1996-765634 19961230 (8)
WO 1995-JP1308 19950630
19961230 PCT 371 date
19961230 PCT 102(e) date
PRAI JP 1994-149681 19940630
JP 1994-172700 19940725
DT Utility
FS Granted
EXNAM Primary Examiner: Kulkosky, Peter F.
LREP Antonelli, Terry, Stout & Kraus, LLP
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 688
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A hair-growing agent comprising **proanthocyanidin** as the active ingredient. The present invention provides a hair-growing agent having strong pharmaceutical effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 23 OF 24 USPATFULL
AN 1999:67382 USPATFULL
TI Method for extraction of **proanthocyanidins** from plant material
IN Nafisi-Movaghar, Karim, Concord, CA, United States
Svanoe, Thomas T., Concord, CA, United States
Seroy, William A., Concord, CA, United States
PA Interhealth Nutraceuticals, Concord, CA, United States (U.S. corporation)

PI US 5912363 19990615
AI US 1997-919805 19970829 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Solola, Taofiq A.
LREP Weseman, Esq., James C.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 539
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for the extraction of **proanthocyanidins** from plant material is disclosed. The method involves heating an aqueous mixture of solid plant material, optionally under increased pressure and reduced oxygen; various separation, filtration and adsorption steps, and the elution of adsorbed **proanthocyanidins** with polar solvent. Optionally, the polar solvent can be reconstituted and recycled into the elution phase of the method, resulting in decreased solvent consumption.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L22 ANSWER 24 OF 24 USPATFULL
AN 97:59236 USPATFULL
TI Cranberry extract and biologically active compounds derived therefrom
IN Walker, Edward B., Ogden, UT, United States
Mickelsen, Jr., Richard A., Ogden, UT, United States
Mickelsen, Jennifer N., Ogden, UT, United States
PA JLB, Inc., Ogden, UT, United States (U.S. corporation)
PI US 5646178 19970708
AI US 1995-473864 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1995-409703, filed on 24 Mar 1995 And Ser. No. US 1994-189889, filed on 1 Feb 1994, now patented, Pat. No. US 5525341 which is a continuation-in-part of Ser. No. US 1992-959222, filed on 9 Oct 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Rollins, John W.
LREP Trask, Britt & Rossa
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 36 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 1675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds isolated from plant materials of the genus Vaccinium, which have biological activity measurable as inhibition with adhesion of bacterial cells to surfaces, are described. The specific compounds include procyanidins, leucocyanin and leucodelphinin, and flavonol glucosides including myricetin-3-pyranoside. An exemplary procyanidin compound is a substituted epicatechin-catechin dimer or other polymer. Also described is an extract prepared from plants of the genus Vaccinium, especially cranberries, which is enriched for anti-adhesion activity. The extract is enriched for polyphenol and flavonoid compounds, lacks detectable amounts of simple sugars, has a very low content of benzoic acid relative to raw cranberries, and lacks significant amounts of anthocyanins. Methods for preparing and for using the extract are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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          1030 PROANTHOCYANIDIN
          1914 PROANTHOCYANIDINS
          2046 PROANTHOCYANIDIN
                 (PROANTHOCYANIDIN OR PROANTHOCYANIDINS)
        257701 PURIFICATION
           841 PURIFICATIONS
        258276 PURIFICATION
                 (PURIFICATION OR PURIFICATIONS)
        241149 PURIFN
           229 PURIFNS
        241251 PURIFN
                 (PURIFN OR PURIFNS)
        383827 PURIFICATION
                 (PURIFICATION OR PURIFN)
        212760 ISOLATION
           904 ISOLATIONS
        213341 ISOLATION
                 (ISOLATION OR ISOLATIONS)
        494707 RESIN
        334809 RESINS
        610404 RESIN
                 (RESIN OR RESINS)
        232977 STYRENE
          4062 STYRENES
        234139 STYRENE
                 (STYRENE OR STYRENES)
         95361 ANIONIC
           236 ANIONICS
         95456 ANIONIC
                 (ANIONIC OR ANIONICS)
         35460 OCTYL
```

```
            4 OCTYLS
        35463 OCTYL
                (OCTYL OR OCTYLS)
        12546 OCTADECYL
            1 OCTADECYLS
        12547 OCTADECYL
                (OCTADECYL OR OCTADECYLS)
       256818 PHENYL
          337 PHENYLS
       257046 PHENYL
                (PHENYL OR PHENYLS)
      1129263 PH
         8331 PHS
      1133054 PH
                (PH OR PHS)
      1319935 PHENYL
                (PHENYL OR PH)
      1968628 WATER
       214554 WATERS
      2018627 WATER
                (WATER OR WATERS)
       167131 ALCOHOL
       125324 ALCOHOLS
       272904 ALCOHOL
                (ALCOHOL OR ALCOHOLS)
       506231 ALC
       164086 ALCS
       591297 ALC
                (ALC OR ALCS)
       686006 ALCOHOL
                (ALCOHOL OR ALC)
       464751 ESTER
       354960 ESTERS
       664106 ESTER
                (ESTER OR ESTERS)
       123934 KETONE
        99996 KETONES
       180647 KETONE
                (KETONE OR KETONES)
L23          1 L21 AND (WATER OR ALCOHOL OR ESTER OR KETONE)

=> dis l23 bib abs

L23  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   1994:532679  CAPLUS
DN   121:132679
TI   Isolation of proanthocyanidins with polystyrene
     resins
IN   Horii, Shoji
PA   Hojo Seiansho Kk, Japan
SO   Jpn. Kokai Tokkyo Koho, 6 pp.
     CODEN: JKXXAF
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
PI   JP 06049053        A2   19940222       JP 1992-202708    19920729
     JP 07062014        B4   19950705
AB   Proanthocyanidins, useful as antioxidants or discoloration
     inhibitors for foods or physiol. active substances (no data), are isolated
     from solns., such as bean-soaking or -boiling water in manuf. of
     bean jam, by adsorption on polystyrene adsorption resins,
     optional washing, drying, and elution with polar solvents with low
```

polarity. Adzuki beans (10 kg) were soaked in H2O for .apprx.16 h, the soaking **water** was treated with Sepabeads sp 850 (adsorption **resin**) at room temp. for .apprx.2 h, dried at .ltoreq.70.degree., and eluted with 60% EtOH at 70.degree. for 2 h to give **proanthocyanidins**.

=> dis hist

(FILE 'HOME' ENTERED AT 14:34:15 ON 21 NOV 2002)

INDEX 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUIRE, BABS, BIOCOMMERCE, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CEN, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, ENCOMPLIT, ENCOMPLIT2, FEDRIP, GENBANK, INSPEC, INSPHYS, INVESTEXT, IPA, ...' ENTERED AT 14:34:43 ON 21 NOV 2002

SEA PROANTHOCYANIDI

L1 QUE PROANTHOCYANIDI

SEA PROANTHOCYANIDIN

398	FILE AGRICOLA
68	FILE ANABSTR
4	FILE APOLLIT
223	FILE BABS
1	FILE BIOCOMMERCE
105	FILE BIOTECHNO
671	FILE CABA
11	FILE CAOLD
2046	FILE CAPLUS
11	FILE CBNB
12	FILE CEABA-VTB
2	FILE CEN
4	FILE CIN
17	FILE COMPENDEX
20	FILE CONFSCI
2	FILE ENCOMPLIT
2	FILE ENCOMPLIT2
17	FILE FEDRIP
8	FILE GENBANK
3	FILE INVESTEXT
32	FILE IPA
96	FILE JICST-EPLUS
8	FILE KOSMET
249	FILE NAPRALERT
1	FILE NIOSHTIC
2	FILE NTIS
31	FILE PAPERCHEM2
455	FILE PASCAL
93	FILE PROMT
3	FILE RAPRA
943	FILE SCISEARCH
1	FILE USAN
1	FILE WSCA

L2 QUE PROANTHOCYANIDIN

SEA L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)

33	FILE AGRICOLA
9	FILE ANABSTR
37	FILE BABS
11	FILE BIOTECHNO
56	FILE CABA

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                1   FILE CAOLD
              245   FILE CAPLUS
                1   FILE CBNB
                6   FILE FEDRIP
               10   FILE IPA
               19   FILE JICST-EPLUS
                2   FILE KOSMET
              182   FILE NAPRALERT
                4   FILE PAPERCHEM2
               94   FILE PASCAL
                5   FILE PROMT
               95   FILE SCISEARCH
L3               QUE L2 AND (ISOLATION OR PURIFICATION AND GRAPE OR APPLE)
                 ---------
                 SEA L3 AND RIBOSYLATION
                 ---------
                 1   FILE CAPLUS
L4               QUE L3 AND RIBOSYLATION
                 ---------

     FILE 'CAPLUS' ENTERED AT 14:42:58 ON 21 NOV 2002
L5             1 S L4
L6          2046 S L2
L7           245 S L3
L8             8 S L7 AND RESIN
L9             2 S L8 AND (STYRENE OR ANIONIC OR OCTADECYL OR OCTYL OR SILICA)
L10            1 S L2 AND RIBOSYLATION
L11            1 S L10 AND INHIBIT?
L12            0 S L2 AND ENTERPTOX?
L13            0 S L2 AND ENTEROTOX?
L14            4 S L2 AND (CHOLERA OR BOTULINUS OR TRAVELER AND DIARRHEA)

     INDEX 'APOLLIT, BABS, CAPLUS, CBNB, CEN, CIN, EMA, IFIPAT, JICST-EPLUS,
     PASCAL, PLASNEWS, PROMT, RAPRA, SCISEARCH, TEXTILETECH, USPATFULL,
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              2046   FILE CAPLUS
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                 2   FILE CEN
                 4   FILE CIN
                 1   FILE EMA
                83   FILE IFIPAT
                96   FILE JICST-EPLUS
               455   FILE PASCAL
                93   FILE PROMT
                 3   FILE RAPRA
               943   FILE SCISEARCH
               202   FILE USPATFULL
                 7   FILE USPAT2
               133   FILE WPIDS
               133   FILE WPINDEX
L15              QUE PROANTHOCYANIDIN
                 ---------
                 SEA L15 AND RIBOSYLATION
                 ---------
                 1   FILE CAPLUS
                 1   FILE WPIDS
                 1   FILE WPINDEX
L16              QUE L15 AND RIBOSYLATION
                 ---------
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L17            1 S L16
L18            8 S L15 AND (ISOLATION OR PURIFICATION)

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     USPAT2, WPIDS, WPINDEX, WTEXTILES' ENTERED AT 15:00:19 ON 21 NOV 2002
               SEA L15 AND (PURIFICATION OR ISOLATION)
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             191   FILE CAPLUS
               4   FILE IFIPAT
              16   FILE JICST-EPLUS
              95   FILE PASCAL
               7   FILE PROMT
              69   FILE SCISEARCH
              76   FILE USPATFULL
               1   FILE USPAT2
               8   FILE WPIDS
               8   FILE WPINDEX
L19            QUE L15 AND (PURIFICATION OR ISOLATION)
              ---------
               SEA L19 AND (RESIN AND STYRENE OR ANIONIC OR OCTYL OR OCTADECYL
              ---------
               3   FILE CAPLUS
               1   FILE PROMT
              24   FILE USPATFULL
               1   FILE USPAT2
               2   FILE WPIDS
               2   FILE WPINDEX
L20            QUE L19 AND (RESIN AND STYRENE OR ANIONIC OR OCTYL OR OCTADECYL
              ---------

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L21           24 S L20
L22           24 S L21 AND (WATER OR ALCOHOL OR ESTER OR KETONE)

     FILE 'CAPLUS' ENTERED AT 15:07:22 ON 21 NOV 2002
L23            1 S L22
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0031-9422/96 $15.00 + 0.00

PROANTHOCYANIDIN POLYMERS WITH ANTISECRETORY ACTIVITY AND PROANTHOCYANIDIN OLIGOMERS FROM *GUAZUMA ULMIFOLIA* BARK

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(*Received* 4 *September* 1995)

Key Word Index—*Guazuma ulmifolia*; Sterculiaceae; bark; proanthocyanidins; tannins; polymers; gel permeation chromatography; NMR; thiolytic degradation; (−)-epicatechin; peracetates; antisecretory activity.

Abstract—Bioassay-guided fractionation of a crude extract of *Guazuma ulmifolia* bark led to the isolation of polymeric proanthocyanidins which inactivated cholera toxin (CT). The average degree of polymerization (DP) of the active compounds ranged from 14.4 to 32.0. The polymers consisted mainly of (−)-epicatechin units. In polymers of a representative fraction, the flavanol units were connected by [4 → 8] bonds and, less frequently, by [4 → 6] bonds. Inhibition of CT by tannins increased with M_r and conformation flexibility of the tannin molecule. Several known procyanidin oligomers were also isolated. ^{1}H NMR shift rules to distinguish between [4 → 8] and [4 → 6] linked proanthocyanidin peracetates, that have been proposed for dimers, were extended to trimers and a tetramer. A further diagnostic shift parameter to determine the interflavanoid bonding position is presented and the conformation of oligomeric proanthocyanidin peracetates is discussed.

INTRODUCTION

Guazuma ulmifolia is used by the Mixe Indians of Oaxaca (Mexico) to treat diarrhoea [1]. Similar uses are known from other areas of Mexico [2]. The ethanol-extract of the bark (C) inhibits cholera toxin-induced secretion in rabbit distal colon mounted in an Ussing chamber. The antisecretory activity is due to the water-soluble part (W) of C. SDS–PAGE analysis shows that the activity is due to a specific interaction of C with the A-subunit of the toxin. The results of SDS–PAGE and Ussing chamber experiments correspond well. Thus, SDS–PAGE appears to be a reliable method for the bioassay-guided fractionation of C and for the investigation of structure–activity relationships of tannins. Preliminary examination indicated that the active compounds were polymeric proanthocyanidins which exclusively contain epicatechin and catechin units [3]. The present paper deals with the purification, characterization and structure–activity relationships of these polymeric proanthocyanidins. In addition, several known oligomeric proanthocyanidins were isolated from the ethyl acetate layer of C.

RESULTS AND DISCUSSION

Bioassay-guided fractionation of W by column chromatography on Sephadex LH-20 with ethanol–water and ethanol–water–acetone mixtures yielded several fractions containing oligomeric and polymeric proanthocyanidins (W1.1–W3.7). Only the fractions which eluted with ethanol–water–acetone (7:7:6) (W3.1–W3.7) showed high activity against CT in SDS–PAGE.

The weight average molecular weight (M_w) and the number average molecular weight (M_N) of the active fractions (W3.1–W3.7) and of some oligomeric fractions (W1.11–W2.7) were determined by gel permeation chromatography (GPC) of the peracetates. The degree of polymerization (DP) was calculated using an average M_r of 500 for one acetylated flavanol unit. To confirm these results M_N was determined by complete thiolytic degradation. The cleavage products were quantified by direct HPLC analysis of the reaction mixture (Table 1). For most of the fractions, GPC indicated lower values for DP than complete thiolysis. These differences can in part be attributed to the use of the unpolar chloroform as eluting solvent [4]. A further reason for the differences between the two methods is the use of linear and rigid polystyrene standards for calibration of GPC in the higher M_r region [5]. The GPC values of fractions W2.2, W3.1, W3.2 and W3.7 were higher than those from thiolysis. The GPC value of W3.1 was almost twice as high as the result obtained by thiolysis. This difference might be attributed to the presence of other linkages besides acid labile [4 → 8] and [4 → 6] interflavanoid bonds. Proanthocyanidins with such unusual linkages are known. For example, Nonaka *et al.* [6] isolated dimeric flavan-3-ols

*Author to whom correspondence should be addressed.

Table 1. $\overline{M_w}$, $\overline{M_N}$ and DP of proanthocyanidins of *Guazuma ulmifolia* bark

Substance fraction	GPC of peracetates				Complete thiolysis	
	$\overline{M_w}$*	$\overline{M_N}$†	DP‡	PD§	$\overline{M_N}$†	DP‡
Epicatechin	710	640	1.3	1.11		
Procyanidin B2	1010	939	1.9	1.08	607	2.1±0
Procyanidin C1	1571	1444	2.9	1.09	866	3.0±0.
W 1.11	3787	2719	5.4	1.39	1788	6.2±0.
W 1.12	4121	3244	6.5	1.27	1903	6.6±0.
W 1.13	3620	2906	5.8	1.25	2018	7.0±0.
W 2.2	7912	5580	11.2	1.42	2623	9.1±0.
W 2.3	5518	4462	8.9	1.24	2450	8.5±0.
W 2.4	4825	3934	7.9	1.23	2479	8.6±0.
W 2.5	4868	4021	8.0	1.21	2680	9.3±0.
W 2.6	5700	4749	9.5	1.20	3026	10.5±0.
W 2.7	7159	5667	11.3	1.26	3458	12.0±0.
W 3.1	22039	15986	32.0	1.38	5100	17.7±0.
W 3.2	10775	8554	17.1	1.26	4466	15.5±0.
W 3.3	9125	7216	14.4	1.26	4869	16.9±0.
W 3.4	10102	7738	15.5	1.31	5042	17.5±1.
W 3.5	10066	7359	14.7	1.37	5157	17.9±1.
W 3.6	13932	10525	21.1	1.32	5791	20.1±1.
W 3.7	15025	10535	21.1	1.43	5071	17.6±0.

*$\overline{M_w}$: weight average molecular weight.
†M_N: number average molecular weight.
‡DP: average degree of polymerization.
§PD: polydispersitivity (M_w/M_N).

linked at the B-rings from green tea leaves. The content of such compounds in tea is drastically increased by polyphenol oxidases during standing in air after harvest [7]. Bonds between two benzene rings might also be generated during extraction of the plant material. Tanaka *et al.* [8] showed that the loss of astringency of persimmon fruits during the anaerobic treatment of the flesh with 30% ethanol is due to condensation of the B-rings of proanthocyanidin oligomers with acetaldehyde to form insoluble polymers. To investigate whether the compounds of W3.1 were generated during isolation we repeated the extraction and separation of the polymeric proanthocyanidins under mild conditions; there were no significant qualitative or quantitative differences compared with the first isolation. Three polymeric fractions of the acetone percolate were analysed by GPC and complete thiolysis. These results and the results of the corresponding fractions of the ethanol extract are given in Table 2. The average DP of AW 3.1, as determined by GPC, was also twice as high as the DP obtained by complete thiolysis. Therefore, formation of these compounds with unusual linkages during extraction can be excluded. They might be either genuine compounds or have been generated during drying of the bark [7].

The nature of the extension units of the proanthocyanidin polymers was deduced by complete thiolysis and HPLC analysis of the cleavage products. The major chain unit is (−)-epicatechin (**1**). (+)-Catechin (**11**) comprises 10% as terminal units and 8% as extension units. The type of interflavanoid bonds of the polymers of fraction W 3.3 was determined by partial thiolysis and HPLC identification and quantification of the dimeric thioethers (−)-epicatechin-[4$\beta \rightarrow$8]-(−)-epicatechin-4β-benzylthioether (**5**) and (−)-epicatechin-[4$\beta \rightarrow$6]-(−)-epicatechin-4β-benzylthioether (**6**). The dimers **5** and **6** were found in a ratio of 3:1. Thus, the flavanol units were connected by [4$\rightarrow$8] bonds and, less frequently, by [4$\rightarrow$6] bonds. According to Porter *et al.* [9], the [4$\rightarrow$6] linkage is cleaved at a slower rate than the [4$\rightarrow$8] bond. Therefore, the frequency of [4$\rightarrow$6] linkages in the polymer would be somewhat overestimated if determined by thiolysis, and may be less than 25%. The structure of the polymers of fraction W 3.3 is illustrated in Fig. 1.

To investigate structure–activity relationships of tannins we compared the activity of procyanidins with different DP and the commercially available gallotan-

Table 2. DP of some polymer fractions of *Guazuma ulmifolia* bark obtained by percolation with acetone–water (7:3) compared with the data for the corresponding fractions of the ethanol extract

Fraction	Complete thiolysis	GPC of peracetates	
		DP	PD
AW 3.1	19.7±1.1	40	1.47
W 3.1	17.7±0.7	32	1.38
AW 3.4	15.7±0.6	15	1.34
W 3.4	17.5±1.6	15.5	1.31
AW 3.6	19.8±1.2	20	1.47
W 3.7	17.6±0.2	21.1	1.43

DP: average degree of polymerization.
PD: polydispersitivity (M_w/M_N).

ark

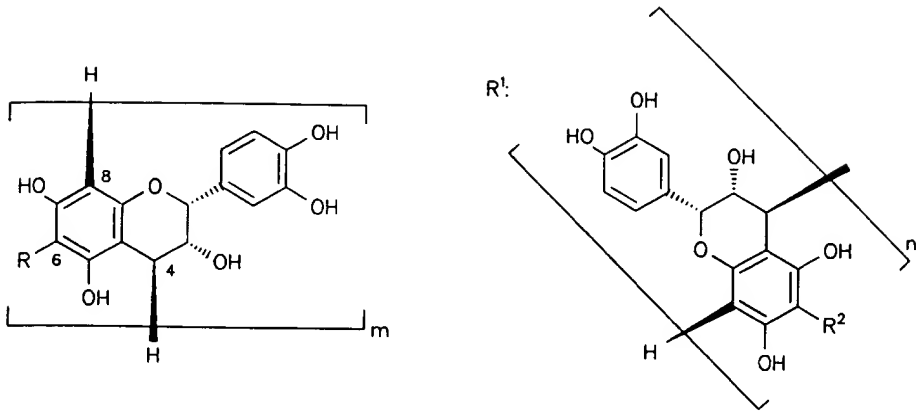
Complete thiolysis	
$\overline{M_N}$†	DP‡
607	2.1±0
866	3.0±0.1
1788	6.2±0.2
1903	6.6±0.5
2018	7.0±0.2
2623	9.1±0.2
2450	8.5±0.3
2479	8.6±0.4
2680	9.3±0.7
3026	10.5±0.1
3458	12.0±0.6
5100	17.7±0.7
4466	15.5±0.1
4869	16.9±0.1
5042	17.5±1.6
5157	17.9±1.4
5791	20.1±1.3
5071	17.6±0.2

ntification and quantifica-
−)-epicatechin-[4β→8]
ioether (5) and (−)-epi-
chin-4β-benzylthioether
found in a ratio of 3:1.
e connected by [4→8]
[4→6] bonds. Accord-
→6] linkage is cleaved at
8] bond. Therefore, the
in the polymer would be
ermined by thiolysis, and
ucture of the polymers of
Fig. 1.
ictivity relationships of
/ity of procyanidins with
cially available gallotan-

ctions of *Guazuma ulmifolia*
acetone–water (7:3) com-
responding fractions of the
tract

GPC of peracetates	
DP	PD
40	1.47
32	1.38
15	1.34
15.5	1.31
20	1.47
21.1	1.43

ization.
).



R = H or R = R¹

m = 1 − 12; n = 0 − 12

m + n = 15

1 − 2 units/molecule are (+)−catechin (11)

Configuration at C−4 of catechin extension units presumably predominantly 3,4−*trans* [29].

R² = H or R² = R¹

Fig. 1. Structure of proanthocyanidins of fraction W3.

nin, tannic acid, using SDS–PAGE. Procyanidins with an average DP of 5 are inactive up to 2500 μg. Procyanidins with an average DP of 10 completely bound the A-subunit of the toxin in a dose of 500–1000 μg. Polymers with an average DP of 15 showed high activity with an active dose of 30 μg. Tannic acid inactivated the A-subunit at 500–1000 μg. Thus, the toxin-binding activity of condensed tannins increased with their M_r. Activity may also be dependent on the conformation flexibility of the tannin molecule as the more flexible tannic acid with an average M_r of 940–1852 is as active as the procyanidin decamer with a M_r of 2900. These findings are in good agreement with earlier general observations on the affinity of tannins for proteins [10].

From the ethyl acetate layer the monomer (−)-epicatechin (**1**), the dimers procyanidin B2 (**3**) and procyanidin B5 (**4**), the trimers procyanidin C1 (**7**), (−)-epicatechin-[4β→6]-(−)-epicatechin-[4β→8]-(−)-epicatechin (**8**) and (−)-epicatechin-[4β→8]-(−)-epicatechin-[4β→6]-(−)-epicatechin (**9**) and the tetramer, (−)-epicatechin-[4β→8]-(−)-epicatechin-[4β→8]-(−)-epicatechin-[4β→8]-(−)-epicatechin (**10**) were isolated. All compounds are known from nature. Compounds **1** and **3** were identified by ^{1}H NMR spectroscopy and OR measurements of the free phenols. The data were consistent with published values [11–14]. Compounds **4** and **7** were identified as their peracetates **4a** and **7a**, respectively. The ^{1}H NMR data for **4a** were in agreement with literature values [15]. The chemical shifts in the ^{1}H NMR spectrum of **7a** were consistent with published values [15] but ^{1}H–^{1}H long-range COSY led to a different assignment of the signals (Table 3). The major difference is the recognition of two rotamers in a ratio of 2:1 in our 400 MHz spectrum. ^{1}H–^{1}H long-range COSY generally detected the correlations between H-4 and H-6, H-8 and H-2, and also between H-2 and H-2′ and H-6′ of the same flavanol unit and thus allowed the assignment of all A- and C-ring protons of both rotamers.

Compound **8** exhibited a $[M+H]^+$ in the FAB-mass spectrum at *m/z* 867, indicating a trimeric procyanidin. Complete thiolysis yielded (−)-epicatechin-4β-benzylthioether (**2**) and (−)-epicatechin (**1**) as the only cleavage products. The lower interflavanoid bond was established as [4→8] by partial thiolysis and ^{1}H NMR identification of procyanidin B2 (**3**). As the ^{1}H NMR data of **8** were not identical with the spectrum of **7**, the upper linkage had to be [4→6]. Trimer **8** was thus identified as (−)-epicatechin-[4β→6]-epicatechin-[4β→8]-(−)-epicatechin, a compound isolated from *Kandelia candel* bark [16] and from Douglas fir (*Pseudotsuga menziesii*) inner bark [17].

The FAB-mass spectrum of compound **9** exhibited a $[M+H]^+$ peak at *m/z* 867 suggesting a trimeric procyanidin. Complete thiolysis yielded (−)-epicatechin-4β-benzylthioether (**2**) and (−)-epicatechin (**1**). The bonding positions were established by partial thiolysis and HPLC identification of procyanidin B5 (**4**) and (−)-epicatechin-[4β→8]-(−)-epicatechin-4β-benzylthioether (**5**) indicating a lower [4→6] linkage and an upper [4→8] linkage. Trimer **9** was thus identified as (−)-epicatechin-[4β→8]-(−)-epicatechin-[4β→6]-(−)-epicatechin, a compound previously isolated from *Rhaphiolepsis umbellata* bark [18].

Complete thiolysis of **10** yielded (−)-epicatechin-4β-benzylthioether (**2**) and (−)-epicatechin (**1**) in a ratio of 3:1 indicating a tetrameric structure. The bonding positions were established by partial thiolysis and HPLC identification of procyanidin C1 (**7**) and (−)-

Table 3. ^{1}H NMR data of compound **7a** in $CDCl_3$ (400 MHz; standard $CHCl_3$ = 7.240 ppm) compared with the data publ by Kolodziej [15] (*ma* = major rotamer, *mi* = minor rotamer; u = upper unit, m = middle unit, l = lower unit)

H	**7a** *ma* δ (J [Hz])	^{1}H–^{1}H long-range-COSY cross-peaks with	**7a** *mi* δ (J [Hz])	^{1}H–^{1}H long-range-COSY cross-peaks with	**7a** [15] δ (J [Hz])
2 u	5.39 *m*	3 u, 4 u, 2′ u, 6′ u	5.69 *br s*	3 u, 4 u, 2′ u, 6′ u	5.37 *m*
3 u	5.35 *m*	2 u, 4 u	4.95 *m*	2 u, 4 u	5.11 *m*
4 u	4.76 *br s*	2 u, 3 u, 6u, 8 u	4.48 *d* (2.0)	2 u, 3 u	4.66 *s*
6 u	6.64 *d* (2.25)	4 u, 8 u	6.24 *d* (2.25)	8 u	5.94 *d* (2.2)
8 u	6.75 *d* (2.25)	4 u, 6 u	5.93 *d* (2.25)	6 u	6.25 *d* (2.2)
2′ u	7.04–7.19 *m*	2 u, 6′ u	7.35 *d* (2.0)	2 u, 6′ u	7.15–7.34 *m*
5′ u	7.04–7.19 *m*	6′ u	7.04–7.28 *m*	6′ u	7.15–7.34 *m*
6′ u	7.04–7.19 *m*	2 u, 2′ u, 5′ u	7.04–7.28 *m*	2 u, 2′ u, 5′ u	7.15–7.34 *m*
2 m	5.35 *m*	3 m, 4 m, 2′ m, 6′ m	4.65 *br s*	3 m, 2′ m	4.76 *s*
3 m	5.39 *m*	2 m, 4 m	5.09 *br s*	2 m, 4 m	5.41 *m* or 5.4
4 m	4.69 *br s*	2 m, 3 m, 6 m	4.65 *br s*	3 m	4.69 *s*
6 m	6.64 *s*	4 m	6.88 *s* or 6.58 *s*		6.64 *s* or 6.6
2′ m	7.04–7.19 *m*	2 m, 6′ m	6.99 *d* (1.8)	2 m, 6′ m	7.15–7.34 *m*
5′ m	7.04–7.19 *m*	6′ m	6.93 *d* (8.25)	6′ m	7.15–7.34 *m*
6′ m	7.04–7.19 *m*	2 m, 2′ m, 5′ m	6.77 *dd* (1.8, 8.25)	2′ m, 5′ m	7.15–7.34 *m*
2 l	5.18 *br s*	3 l, 4 l α + β, 2′ l, 6′ l	5.10 *br s*	3 l, 4 l α + β, 2′ l	5.19 *s*
3 l	5.46 *m*	2 l, 4 l α + β	5.39 *m*	2 l, 4 l α + β	5.47 *m* or 5.4
4 l α	2.94 *br d* (18.0)	2 l, 3 l, 4 l β	2.88*	2 l, 3 l, 4 l β	3.00 *m*
4 l β	3.07 *dd* (5.0, 18.0)	2 l, 3 l, 4 l α	3.02*	2 l, 3 l, 4 l α	3.00 *m*
6 l	6.69 *s*		6.58 *s* or 6.88 *s*		6.69 *s* or 6.64
2′ l	7.28 *d* (1.8)	2 l, 6′ l	7.25†	2 l, 6′ l	7.15–7.34 *m*
5′ l	7.04–7.19 *m*	6′ l	7.04–7.28 *m*	6′ l	7.15–7.34 *m*
6′ l	7.04–7.19 *m*	2 l, 2′ l, 5′ l	7.04–7.28 *m*	2′ l, 5′ l	7.15–7.34 *m*
OAc	1.36–2.35 *m*		1.36–2.35 *m*		1.37–2.37 *m*

*Overlapping with *ma*.
†Overlapping with $CHCl_3$.

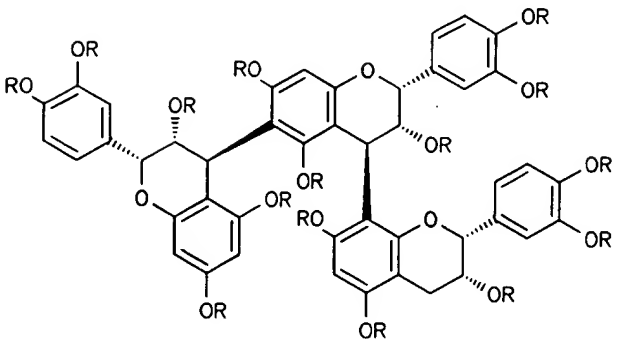
epicatechin - [4$\beta \rightarrow$8] - (−) - epicatechin - 4β - benzylthioether (**5**). With the formation of trimer **7** the lower two linkages were identified as [4 → 8]. As **5** was the only dimeric thioether formed by thiolysis, the upper linkage also had to be [4 → 8]. Tetramer **10** was thus identified as (−)-epicatechin-[4$\beta \rightarrow$8]-(−)-epicatechin - [4$\beta \rightarrow$8] - (−) - epicatechin - [4$\beta \rightarrow$8] - epicatechin, a compound previously isolated from *Cinnamomum cassia* bark [19].

For proanthocyanidin peracetates, shift parameters to distinguish between [4 → 8]- and [4 → 6]-linked dimers have been published. The upper A-ring signals of [4 → 8]-linked dimeric peracetates are shifted upfield to *ca* δ 6.1, whereas the upper A-ring protons of [4 → 6]-linked dimers resonate near δ 6.7 [20, 21]. In addition, H-2(l) of [4 → 8]-linked dimeric peracetates resonates between δ 4.37 and δ 5.01, whereas H-2(l) of [4 → 6]-linked dimers resonates between δ 5.04 and 5.35 [22]. To explain the upfield shifts of H-6(u), H-8(u) and H-2(l) of [4 → 8]-linked dimeric peracetates a cc formation with the B-ring of the lower unit lying abo the A-ring of the upper unit has been suggested [2(The validity of these parameters has not been inves gated systematically for trimeric and tetrameric perac tates. Therefore, compounds **7–10** were converted in their peracetates and analysed by ^{1}H NMR and ^{1}H–^{1} long-range COSY. All but **8a** displayed rotation isomerism. The spectrum of **8a** consisted of only o set of signals. The two doublets of H-6(u) and H-8(were located at δ 6.57 and 6.65, respectively, cor sponding well with the chemical shifts of the sar protons of [4 → 6]-linked dimeric peracetates [21]. T chemical shift for H-2(m) of **8a** (δ 5.46) is al consistent with the H-2(l) chemical shift of [4 → 6 linked dimers [22]. The chemical shifts for the upp A-ring protons at δ 5.93 and δ 6.24, and for H-2(m) δ 4.65 of the minor rotamer of **7a** were in accordan with the chemical shifts of [4 → 8]-linked dime

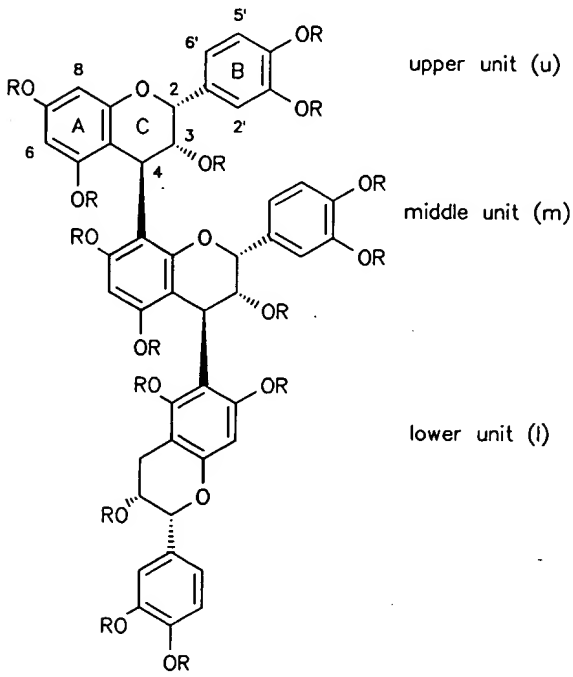
pared with the data published
: unit, l = lower unit)

OSY ith	7a [15] δ (J [Hz])
. 6′ u	5.37 *m*
	5.11 *m*
	4.66 *s*
	5.94 *d*
	(2.2)
	6.25 *d*
	(2.2)
	7.15–7.34 *m*
	7.15–7.34 *m*
l	7.15–7.34 *m*
	4.76 *s*
	5.41 *m* or 5.47 *m*
	4.69 *s*
	6.64 *s* or 6.69 *s*
	7.15–7.34 *m*
	7.15–7.34 *m*
	7.15–7.34 *m*
; 2′ l	5.19 *s*
:	5.47 *m* or 5.41 *m*
	3.00 *m*
	3.00 *m*
	6.69 *s* or 6.64 *s*
	7.15–7.34 *m*
	7.15–7.34 *m*
	7.15–7.34 *m*
	1.37–2.37 *m*

imeric peracetates a con-
the lower unit lying above
t has been suggested [20].
eters has not been investi-
eric and tetrameric perace-
7–10 were converted into
d by ^{1}H NMR and ^{1}H–^{1}H
t **8a** displayed rotational
8a consisted of only one
blets of H-6(u) and H-8(u)
6.65, respectively, corre-
emical shifts of the same
meric peracetates [21]. The
of **8a** (δ 5.46) is also
chemical shift of [4→6]-
emical shifts for the upper
l δ 6.24, and for H-2(m) at
of **7a** were in accordance
of [4→8]-linked dimers



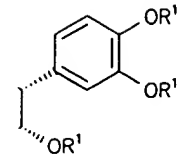
8: R = H
8a: R = Ac



9: R = H
9a: R = Ac

[21, 22]. The spectrum of **9a** showed two major pairs of doublets for H-6(u) and H-8(u) with equal intensities. Probably, there were minor rotamers or other conformers present, as the spectrum showed further small A-ring signals and line-broadening in the heterocyclic region. One major pair of doublets resonated at δ 6.02 and 6.29, respectively, corresponding well with the chemical shifts of [4→8]-linked dimers [21]. Unfortunately, owing to poor resolution of the spectrum the assignment of the signals of H-2 and H-3 of the middle unit of **9a** was not possible. Therefore, the shift parameter for H-2 could not be verified for **9a**. The spectrum of **10a** was sharp and consisted of two sets of signals attributable to two rotamers in a ratio of 3:2. The A-ring protons of the minor rotamer resonated at δ 5.87 and 6.23, respectively. H-2 of the second upper unit of the minor rotamer was attributed to the broad singlet at δ 4.54. Thus, the validity of the shift rules for dimeric peracetates was also confirmed for the tetramer **10a**.

Beyond these known shift parameters a further remarkable feature of the minor rotamers of **7a** and **10a** was observed. H-2′, H-5′ and H-6′ of the second upper units were distinctly shifted upfield resonating between δ 6.67 and 6.99 (for individual chemical shifts see Table 3 and Experimental). These data are consistent with the conformation described above; not only are the upper A-ring protons in the shielding region of the



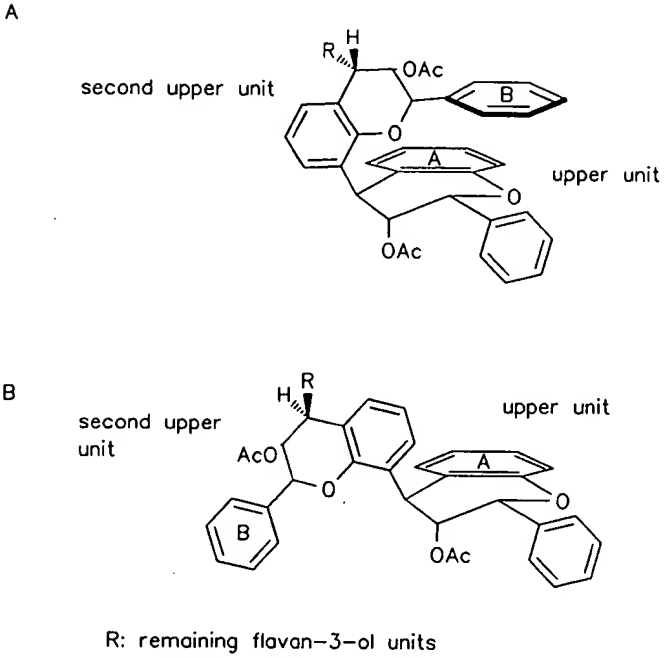


Fig. 2. Suggested conformations of oligomeric proanthrocyanidin peracetates (aromatic groups are omitted).

cond upper unit (Fig. 2B). nits of both rotamers are ecting away from the next ers, in oligomeric perace- nkage the rotamer with the rotamer or occurs, at best, as the B-conformer. In with the upper linkage ears to be so strong that on.

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preparation of the EtOH- *ca* 15-year-old tree was in Oaxaca, Mexico, and am. (Sterculiaceae) by M. en (no. Heinrich and An- ed at the herbarium of the Biologie, Freiburg, Ger- l Herbarium of Mexico ercolate, stem bark of a *ca* ested in March 1994 in nen is deposited at the Pharmazeutische Biologie, 4).

recorded at 400 MHz; δ (ppm). 2D NMR spectra l-long-range (l.r.) COSY) of standard COSY pulse optimized for coupling of

3 Hz. FAB-MS were obtained in the positive mode; matrix: glycerol–HOAc; acceleration 3 kV.

HPLC. Eurosphere C-18 column (5 μm, 250 × 4 mm, Knauer) protected with a guard cartridge packed with the same material. Detection: UV 280 nm. Mobile phase A: MeOH–MeCN–H_2O (5:4:1); mobile phase B: 0.02% TFA in H_2O.

CC. Sephadex LH-20, 25–100 μm (Pharmacia) and MCI-gel CHP-20P, 75–150 μm (Mitsubishi Chem. Ind.).

TLC. Silica gel 60 F_{254} (Merck); EtOAc–HCOOH–H_2O (18:1:1) (system A); detection vanillin–H_2SO_4 and $FeCl_3$. Cellulose (Merck); HOAc–HCl–H_2O (30:3:10) (Forestal); detection VIS.

Extraction and isolation. Air-dried and powdered bark (1040 g) was extracted with cold EtOH 70% (5 l, 3 min, Ultra turrax). After filtration, the bark was refluxed with EtOH 96% (5 l, 20 min) and EtOH 70% (5 l, 20 min, ×2). EtOH was removed *in vacuo* (40°) and the aq. residues of the hot and cold extracts combined and freeze-dried to yield 200 g crude extract (C). C (154 g) was dissolved in H_2O (2300 ml), washed with CH_2Cl_2 (3 × 2300 ml) and extracted with EtOAc (3 × 2300 ml, 1 × 1150 ml). After removal of solvents, the residues were lyophilized to yield 5.6 g CH_2Cl_2-layer (D), 11.9 g EtOAc-layer (E) and 132.8 g H_2O-layer (W). W (18 g) was chromatographed with EtOH 50% (5 l) on Sephadex LH-20 (column 440 × 37 mm). Frs were monitored by TLC in system A. The eluate was combined to 13 frs (W1.1–W1.13) of 100–300 ml at the beginning and 500–1000 ml at the end of CC. Frs W1.1 and W1.2 contained polysaccharides and W1.3–W1.13 contained oligomeric procyanidins. The remaining substances (6.2 g) were washed off the column with 2500 ml Me_2CO–H_2O (7:3) and further separated on Sephadex LH-20 with EtOH–H_2O–Me_2CO (9:9:2) (5100 ml, column 480 × 37 mm) to yield seven frs of 400–1000 ml (W2.1–W2.7). The remaining substances (3.3 g) were washed off the column with 2300 ml Me_2CO–H_2O (7:3) and were further chromatographed on Sephadex LH-20 with EtOH–H_2O–Me_2CO (7:7:6) (1800 ml, column 410 × 37 mm) to give six frs of 250–400 ml (W3.1–W3.6). The remaining substances (0.1 g) were washed off the column with 1500 ml Me_2CO–H_2O (7:3) (= W3.7). W3.1–W3.7 contained polymeric procyanidins.

Air-dried and powdered bark (111 g) was percolated in the dark at 10° with 1300 ml Me_2CO–H_2O (7:3) saturated with N_2. Me_2CO was removed *in vacuo* and the aq. residue freeze-dried to yield 21 g Me_2CO percolate (A). Liquid–liquid extraction of A (19 g) as described for the crude extract (C) gave 0.4 g CH_2Cl_2 layer (AD), 1.6 g EtOAc layer (AE) and 16 g H_2O layer (AW). AW was chromatographed on Sephadex LH-20 as described for W but all solvents were saturated with N_2. Frs AW3.1–AW3.6 contained polymeric procyanidins.

E was chromatographed on Sephadex LH-20 (580 × 34 mm) with EtOH 96% to yield 700 mg (−)-epicatechin (**1**) (920–1220 ml), 1120 mg procyanidin B2 (**3**) (1320–2000 ml) and 315 mg fr. E1.8 (2700–3300 ml). The remaining substances (2.14 g) were washed off the column with Me_2CO–H_2O 8:2 (= E2). E2 was further chromatographed on Sephadex LH-20 (580 × 34 mm) with EtOH 50% to yield 134 mg (−)-epicatechin-[4β → 6]-(−)-epicatechin-[4β → 8]-(−)-epicatechin (**8**) (2310–2625 ml) and 411 mg fr. E 2.6 (2755–3415 ml). Fr. E 1.8 was chromatographed on MCI-gel

(390 × 17.5 mm) with MeOH (35 → 45%, 5% steps); 16-ml frs were collected to give 102 mg procyanidin C1 (**7**) (frs 11–30) and fr. 78. Fr. 78 was further purified on MCI-gel (390 × 17.5 mm) with MeOH 50% (16-ml frs) to yield 27 mg procyanidin B5 (**4**) (frs 13–20). Fr. E 2.6 was chromatographed on MCI-gel (330 × 19 mm) with MeOH 25% 400 ml and MeOH (30 → 50%, 5% steps, 200 ml each); 20 ml frs were collected. Frs 48–51 yielded 49 mg (−)-epicatechin-[4β → 8]-(−)-epicatechin-[4β → 8]-(−)-epicatechin-[4β → 8]-(−)-epicatechin (**10**) and frs 57–60 contained 26 mg (−)-epicatechin-[4β → 8]-(−)-epicatechin-[4β → 6]-(−)-epicatechin (**9**). Note, in the following u = upper unit, um = upper middle unit, lm = lower middle unit, l = lower unit.

(−)-*Epicatechin* (**1**). $[\alpha]_D^{27}$ −30.9° (Me_2CO; *c* 1.18), ref. [12]: $[\alpha]_D$ −57.6° (Me_2CO; *c* 2.1). Difference may be due to unspecific impurities. ^1H NMR data consistent with published values [11].

Procyanidin B2 (**3**). $[\alpha]_D^{28}$ +31° (Me_2CO; *c* 0.9), ref. [14]: $[\alpha]_D^{25}$ +35.5° (Me_2CO; *c* 1.0). FAB-MS: *m/z* 579 $[M+H]^+$. ^1H NMR data consistent with published values [13]. Complete prep. thiolysis of **3** yielded **1** and **2**.

Procyanidin B5 (**4**). $[\alpha]_D^{27}$ +108° (Me_2CO; *c* 0.93), ref. for (+)-epicatechin-[4α → 6]-(+)-epicatechin [23]: $[\alpha]_D^{26}$ −105° (Me_2CO; *c* 0.993). ^1H NMR (Me_2CO-d_6, standard Me_2CO-d_5 = 2.04 ppm): δ 2.66 (1H, *dd*, *J* = 2.1, 16.5 Hz, H-4α(l)), 2.80 (1H, *dd*, *J* = 4.2, 16.5 Hz, H-4β(l)), 4.08 (1H, *br s*, H-3(u)), 4.17 (1H, *br s*, H-3(l)), 4.66 (1H, *d*, *J* = 1.8 Hz, H-4(u)), 4.84 (1H, *br s*, H-2(l)), 4.98 (1H, *br s*, H-2(u)), 6.05 (1H, *s*, H-8(l)), 6.08 and 6.10 (1H each, *d*, *J* = 2.55 Hz, H-6(u) and H-8(u)), 6.73 (1H, *dd*, *J* = 1.8, 8.25 Hz, H-6′(u), 6.76 (1H, *d*, *J* = 8.25 Hz, H-5′(u)), 6.78 (1H, *d*, *J* = 8.25 Hz, H-5′(l)), 6.85 (1H, *dd*, *J* = 1.8, 8.25 Hz, H-6′(l)), 6.98 (1H, *d*, *J* = 18 Hz, H-2′(u)), 7.06 (1H, *d*, *J* = 1.8 Hz, H-2′(l)). Assignment of signals according to ^1H–^1H-l.r.-COSY. The 100 MHz ^1H NMR data of **4** in Me_2CO-d_6 [14] in agreement with our spectrum. ^1H NMR data of the peracetate of **4** (**4a**) were consistent with published values [15].

Procyanidin C1 (**7**). $[\alpha]_D^{27}$ +76.4° (Me_2CO; *c* 0.86), ref. [14]: $[\alpha]_D^{28}$ +75.2° (Me_2CO; *c* 0.87). FAB-MS: *m/z* 867 $[M+H]^+$. ^1H NMR (Me_2CO-d_6, standard Me_2CO-d_5 = 2.04 ppm): δ *ca* 2.7–2.8 (1H, overlapping with HDO, H-4α(l)), 2.93 (1H, *dd*, *J* = 5.4, 17.0 Hz, H-4β(l)), 4.07 (2H, *br s*, H-3(u), H-3(m)), 4.33 (1H, *br s*, H-3(l)), 4.80 and 4.82 (2H, 2 *br s*, H-4(u), H-4(m)), 5.06 and 5.15 (3H, 2 *br s*, H-2(u), H-2(m), H-2(l)), 5.96–6.03 (4H, *m*, H-6(u), H-8(u), H-6(m), H-6(l)), 6.68–6.80 (6H, *m*, H-5′(u), H-5′(m), H-5′(l), H-6′(u), H-6′(m), H-6′(l)), 6.95, 7.00 and 7.17 (1H each, 3 *br s*, H-2′(u), H-2′(m), H-2′(l)). 100 MHz ^1H NMR data of **7** in Me_2CO-d_6 [14] in agreement with our spectrum. Partial prep. thiolysis of **7** yielded **1**, **2**, **3** and **5**. ^1H NMR data of peracetate of **7** (**7a**) in Table 3.

(−) - *Epicatechin* - [4β → 6] - (−) - *epicatechin* - [4β → 8]-(−)-*epicatechin* (**8**). $[\alpha]_D^{26}$ +102.8° (Me_2CO; *c* 1.6), ref. [16]: $]\alpha]_D^{28}$ +138.0° (Me_2CO; *c* 1.0). Difference may be due to unspecific impurities. MS: *m/z* 867 $[M+H]^+$. ^1H NMR (Me_2CO-d_6 dard Me_2CO-d_5 = 2.04 ppm): δ 2.68 (1H, *br* 4α(l)), *ca* 2.9 (1H, overlapping with HDO, H- 3.95 (1H, *m*, H-3(u) or H-3(m)), 3.98 (1H, *br s*, l or H-3(u)), 4.26 (1H, *m*, H-3(l)), 4.58 (1H, *br s*, or H-4(m)), 4.68 (1H, *br s*, H-4(m) or H-4(u)) (3H, *br s*, H-2(u), H-2(m), H-2(l)), 5.95–6.10 (4 H-6(u), H-8(u), H-8 (m), H-6(l)), 6.65–6.86 (6 5′(u), H-5′(m), H-5′(l), H-6′(u), H-6′(m), H- 6.98, 7.02 and 7.09 (1H each, 3 *br s*, H-2′(u), H- H-2′(l)). 100 MHz ^1H NMR data of **8** in Me_2C D_2O [16] showed small differences from our these deviations can be attributed to the addit D_2O and to the poor resolution of the 10(spectrum. Complete analytical thiolysis yielded **2** in a ratio of 2:1. Partial prep. thiolysis of **8** yiel **2**, **3** and **6**. Acetylation yielded the peracetate NMR ($CDCl_3$, standard $CHCl_3$ = 7.24 ppm): δ 2.38 (45H, 15 × OAc), 2.88–3.12 (2H, *m*, not res H-4α(l), H-4β(l)), 4.39 (1H, *br s*, H-4(m)), 4.4 *d*, *J* = 1.6 Hz, H-4(u)), 4.94 (1H, *m*, H-3(u)), 5.1 *br s*, H-2(l)), 5.27 (1H, *m*, H-3(m)), 5.46 (2H, H-2(m), H-3(l)), 5.67 (1H, *br s*, H-2(u)), 6.47 (H-6(l)), 6.57 (1H, *d*, *J* = 2.25 Hz, H-6(u)), 6.65 (*J* = 2.25 Hz, H-8(u)), 6.84 (1H, *s*, H-8(m)), 7.04 (9H, *m*, H-2′(u), H-2′(m), H-2′(l), H-5′(u), H- H-5′(l), H-6′(u), H-6′(m), H-6′(l)).

(−) - *Epicatechin* - [4β → 8] - (−) - *epicate* [4β → 6]-(−)-*epicatechin* (**9**). $[\alpha]_D^{26}$ +123.9° (M *c* 1.64), ref. [18]: $[\alpha]_D^{18}$ +126.8° (Me_2CO; *c* FABMS: *m/z* 867 $[M+H]^+$. ^1H NMR (Me_2C standard Me_2CO-d_5 = 2.04 ppm): δ *ca* 2.7–2.9 overlapping with HDO, H-4 α(l), H-4β(l)), 4.0 *br s*, H-3(u) or H-3(m)), 4.19 (2H, *br s*, H-3(H-3(u) or H-3(m)), 4.75 and 4.83 (1H each, H-4(u), H-4(m)), 4.85 (1H, *s*, H-2(l)), 5.11 (2H, H-2(u), H-2(m)), 5.98–6.07 (4H, *m*, H-6(u), H H-6(m), H-8(l)), 6.72–6.85 (6H, *m*, H-5′(u), H- H-5′(l), H-6′(u), H-6′(m), H-6′(l)), 6.99–7.07 (3 H-2′(u), H-2′(m), H-2′(l)). 100 MHz ^1H NMR da in Me_2CO-d_6 [18] in agreement with our spectr part of the spectrum is presented; the signals re are identical to our spectrum but because of broadening in the published spectrum an exact parison was not possible. Complete analytical thi yielded **2** and **1** in a ratio of 2:1. Partial ana thiolysis yielded **1**, **2**, **4** and **5**. Acetylation yield peracetate **9a**. ^1H NMR ($CDCl_3$, standard CH 7.24 ppm, *A* = rotamer A, *B* = rotamer B, ratio δ 1.23–2.35 (45H, 15 × OAc), 2.7–3.08 (2H, 4α(l) *A* and *B*, H-4β(l) *A* and *B*), 4.05 (0.5H, H-4(m) *A* or *B*), 4.34 (0.5 H, *br s*, H-4(m) *B* or *A* (0.5H, *d*, *J* = 2.4 Hz, H-4(u) *B*), 4.69 (0.5H, H-4(u) *A*), 4.94 (0.5H, *m*, H-3(u) *B*), 5.12 (0.5H H-2(l) *A* or *B*), 5.16 (1H, *br s*, H-2(l) *B* or *A*) (0.5H, *br s*, H-2(u) *A*), 5.49 (0.5H, *br s*, H-3(u) *A* (0.5H, *br s*, H-2(u) *B*), 6.02 (0.5H, *d*, *J* = 2. H-8(u) *B*), 6.29 (0.5H, *d*, *J* = 2.25 Hz, H-6(u) *B*, (1H, *s*, H-6(m) *A* and H-6(m) *B* or H-8(l) *A* or

specific impurities. FAB-
NMR (Me_2CO-d_6, stan-
δ 2.68 (1H, *br d*, H-
ng with HDO, H-4β(l)),
)), 3.98 (1H, *br s*, H-3(m)
.)), 4.58 (1H, *br s*, H-4(u)
H-4(m) or H-4(u)), 4.93
-2(l)), 5.95–6.10 (4H, *m*,
5(l)), 6.65–6.86 (6H, H-
5'(u), H-6'(m), H-6'(l)),
3 *br s*, H-2'(u), H-2'(m),
data of **8** in Me_2CO-d_6-
ferences from our data;
buted to the addition of
dution of the 100 MHz
thiolysis yielded **2** and **1**
. thiolysis of **8** yielded **1**,
ded the peracetate **8a**. ^1H
Cl_3 = 7.24 ppm): δ 1.25–
3.12 (2H, *m*, not resolved,
br s, H-4(m)), 4.48 (1H,
1H, *m*, H-3(u)), 5.14 (1H,
H-3(m)), 5.46 (2H, *br s*,
s, H-2(u)), 6.47 (1H, *s*,
Hz, H-6(u)), 6.65 (1H, *d*,
H, *s*, H-8(m)), 7.04–7.51
l-2'(l), H-5'(u), H-5'(m),
5'(l)).

·8] - (−) - *epicatechin* -
$[\alpha]_D^{26}$ +123.9° (Me_2CO;
26.8° (Me_2CO; *c* 1.15).
. ^1H NMR (Me_2CO-d_6,
)m): δ *ca* 2.7–2.9 (2H,
α(l), H-4β(l)), 4.09 (1H,
9 (2H, *br s*, H-3(l) and
l 4.83 (1H each, 2*br s*,
H-2(l)), 5.11 (2H, *br s*,
(4H, *m*, H-6(u), H-8(u),
5H, *m*, H-5'(u), H-5'(m),
5'(l)), 6.99–7.07 (3H, *m*,
) MHz ^1H NMR data of **9**
ent with our spectrum. A
nted; the signals resolved
m but because of line-
spectrum an exact com-
nplete analytical thiolysis
of 2:1. Partial analytical
5. Acetylation yielded the
Cl_3, standard $CHCl_3$ =
= rotamer B, ratio 1:1):
:), 2.7–3.08 (2H, *m*, H-
nd *B*), 4.05 (0.5H, *br s*,
br s, H-4(m) *B* or *A*), 4.46
) *B*), 4.69 (0.5H, *br s*,
3(u) *B*), 5.12 (0.5H, *br s*,
s, H-2(l) *B* or *A*), 5.22
).5H, *br s*, H-3(u) *A*), 5.66
2 (0.5H, *d*, J = 2.25 Hz,
2.25 Hz, H-6(u) *B*), 6.62
B or H-8(l) *A* or H-8(l)
B), 6.65 (0.5 H, *s*, H-6(m) *B* or H-8(l) *A* or H-8(l) *B*), 6.68 (0.5H, *d*, J = 2.25 Hz, H-6(u) *A*), 6.73 (0.5H, *d*, J = 2.25 Hz, H-8(u) *A*), 6.76 (0.5H, *s*, H-6(m) *B* or H-8(l) *A* or H-8(l) *B*), 6.80–7.36 (9H, *m*, H-2'(u), H-2'(m), H-2'(l) *A* and *B*, H-5'(u), H-5'(m), H-5'(l) *A* and *B*, H-6'(u), H-6'(m), H-6'(l) *A* and *B*). Unequivocal assignment of H-2(m) *A* and *B* and of H-3(m) *A* and *B* not possible.

(−) - *Epicatechin* - [4β→8] - (−) - *epicatechin* - [4β→8] - (−) - *epicatechin* - [4β→8] - (−) - *epicatechin* (**10**). $[\alpha]_D^{26}$ +109.5° (Me_2CO; *c* 1.23), ref. [19]: $[\alpha]_D^{23}$ +89.2° (Me_2CO; *c* 0.9). ^1H NMR (Me_2CO-d_6, standard Me_2CO-d_5 = 2.04 ppm): δ *ca* 2.7–2.8 (1H, overlapping with HDO, H-4α(l)), 2.94 (1H, *dd*, J = 4.5, 16.5 Hz, H-4β(l)), 4.08 (1H, *br s*) and 4.12 (2H, *br s*, H-3(u), H-3(um), H-3(lm)), 4.35 (1H, *br s*, H-3(l)), 4.83 (2H, *br s*) and 4.90 (1H, *br s*, H-4(u), H-4(um), H-4(lm)), 5.07 (1H, *br s*), 5.15 (1H, *br s*) and 5.29 (2H, *br s*, H-2(u), H-2(um), H-2(lm), H-2(l)), 5.96–6.03 (5H, *m*, H-6(u), H-8(u), H-6(um), H-6(lm), H-6(l)), 6.68–6.83 (8H, *m*, H-5'(u), H-5'(um), H-5'(lm), H-5'(l), H-6'(u), H-6'(um), H-6'(lm), H-6'(l)), 6.95, 6.99, 7.08 and 7.17 (1H each, 4*br s*, H-2'(u), H-2'(um), H-2'(lm), H-2'(l)). 100 MHz ^1H NMR data of **10** in Me_2CO-d_6 [19] in agreement with our spectrum. Complete analytical thiolysis yielded **2** and **1** in a ratio of 3:1. Partial analytical thiolysis yielded **1**, **2**, **3**, **5** and **7**. Acetylation yielded the peracetate **10a**. ^1H NMR ($CDCl_3$, standard $CHCl_3$ = 7.24 ppm, *ma* = major rotamer, *mi* = minor rotamer, ratio 3:2): δ 1.33–2.36 (60H, 20 × OAc *ma* and *mi*), 2.93 (0.4H, *br d*, J = 18 Hz, H-4α(l)*mi*), 2.94 (0.6H, *br d*, J = 18 Hz, H-4α(l)*ma*), 3.04 (0.4H, *dd*, J = 4.5, 18 Hz, H-4β(l)*mi*), 3.06 (0.6H, *dd*, J = 4.6, 18 Hz, H-4β(l)*ma*), 4.50 (0.4H, *d*, J = 2.4 Hz, H-4(u)*mi*), 4.54 (0.4H, *br s*, H-2(um)*mi*), 4.60 (0.4H, *br s*, H-4(lm)*mi*), 4.65 (0.6H, *br s*, H-4(lm)*ma*), 4.75 (0.6H, *br s*, H-4(u)*ma*), 4.78 (0.4H, *br s*, H-4(um)*mi*), 4.82 (0.6H, *br s*, H-4(um)*ma*), 4.95 (0.4H, *m*, H-3(u)*mi*), 5.13 (0.4H, *br s*, H-3(um)*mi*), 5.18 (1H, 2 *br s*, H-2(l)*ma* and *mi*), 5.26 (1H, *br s*, H-2(lm)*ma*, H-3(lm)*mi*), 5.29 (0.6H, *m*, H-3(u)*ma*), 5.31 (0.6H, *m*, H-3(lm)*ma*), 5.33 (1*H*, *br s*, H-3(um)*ma*, H-2(lm)*mi*), 5.42 (1.2H, *br s*, H-2(u)*ma*, H-2(um)*ma*), 5.46 (1H, *br s*, H-3(l)*ma* and *mi*), 5.72 (0.4 H, *br s*, H-2(u)*mi*), 5.87 (0.4H, *d*, J = 2.25 Hz, H-8(u)*mi*), 6.23 (0.4H, *d*, J = 2.25 Hz, H-6(u)*mi*), 6.57 (0.4H, *s*, H-6(l)*mi*), 6.60 (0.4H, *s*, H-6(lm)*mi*), 6.63 (0.6H, *s*, H-6(l)*ma*), 6.63 (0.6H, *d*, J = 2.25 Hz, H-6(u)*ma*), 6.67 (0.4H, *dd*, J = 2.0, 8.25 Hz, H-6'(um)*mi*), 6.69 (0.6H, *s*, H-6(lm)*ma*), 6.73 (0.6H, *s*, H-6(um)*ma*), 6.75 (0.6H, *d*, J = 2.25 Hz, H-8(u)*ma*), 6.87 (0.4H, *s*, H-6(um)*mi*), 6.91 (0.4H, *br s*, H-2'(um)*mi*) 6.92 (0.4H, *d*, J = 8.25 Hz, H-5'(um)*mi*), 6.95–7.34 (10.8H, *m*, H-2'(um)*ma*, H-2'(u), H-2'(lm), H-2'(l)*ma* and *mi*, H-5'(um)*ma*, H-5'(u), H-5'(lm), H-5'(l)*ma* and *mi*, H-6'(um)*ma*, H-6'(u), H-6'(lm), H-6'(l)*ma* and *mi*).

GPC. LKB Bromma HPLC-pump using a Knauer dual detector (RI and UV, 280 nm). Peracetylated proanthocyanidins were analysed on 10^3, 10^4, 10^5 and 10^6 Å PL-gel columns (300 × 7.7 mm; Polymer Lab.) connected in series. Elution was isocratic with $CHCl_3$ at 0.5, 0.75 and 1 ml min^{-1}, respectively. The system was calibrated with epicatechin peracetate (M_r 500), procyanidin B2 peracetate (M_r 998), procyanidin C1 peracetate (M_r 1496) and polystyrene standards (M_r 794, 2000, 4000, 10 300, 50 000 and 110 000). The calibration curve was generated using cubic splines.

$\overline{M_N}$ determination by complete thiolysis. Sample (3 mg) were dissolved in 300 μl EtOH 96%, 30 μl toluene-α-thiol and 15 μl HOAc were added under N_2. The sealed vial was kept for 120 hr at 94°. This mixt. was directly analysed by HPLC using the following elution conditions: flow rate 1 ml min^{-1}; mobile phase A, MeOH–MeCN–H_2O (5:4:1); mobile phase B, 0.02% TFA in H_2O; linear gradient from 30 to 70% A in 28 min, isocratic for 4 min, from 70 to 100% A in 2 min, followed by washing for 11 min and reconditioning of the column. Calibration was performed using (−) -epicatechin-4β-benzylthioether (obtained by complete thiolysis of **3**) and (−)-epicatechin (Fluka AG) as standards; R_t 28.0 and 8.8 min, respectively. Standard solns with molar ratios ((−)-epicatechin-4β-benzylthioether:(−)-epicatechin) of 28.7:1, 17.8:1, 10.9:1 and 1:1 were measured and calibration factors for the different ratios calculated. The calibration factor (equimolecular ratio of peak areas of epicatechin-4β-benzylthioether to epicatechin) varied between 1.02 for the 1:1-standard and 0.65 for the 28.7:1-standard. The calibration factor for a certain polymer fr. was selected depending on its GPC result. Values are means of three replicated injections.

Identification of extension units by complete thiolysis. The products of complete thiolysis of polymeric frs were identified by HPLC addition analysis with authentic samples. The only cleavage products were (+)-catechin (**11**) (R_t = 6.4 min), (−)-epicatechin (**1**) (R_t = 8.8 min), (+)-catechin-4β-benzylthioether (**12**) (R_t = 25.9 min) and (−)-epicatechin-4β-benzylthioether (**2**) (R_t = 28.0 min). The peak of (+) - catechin - 4α - benzylthioether (**13**) (R_t = 24.2 min) was too small to be detected unequivocally. Therefore, this cleavage product was neglected. Authentic samples: **1** from Fluka AG; **11** from Roth; **2** obtained by complete thiolysis of **3**; **12** and **13** obtained by complete thiolysis of proanthocyanidins from *Quercus petraea* bark [24]. During thioacidolysis, epimerization may occur [25]. Therefore, we determined the rate of conversion of **1**, **2** and **11**. Under our experimental conditions only **1** was epimerized to 2%. This rate was taken into account for estimation of the polymer composition.

Acetylation. Sample (25 mg) were dissolved in 1 ml pyridine and 1 ml Ac_2O. After stirring at room temp. for 48 hr, excess reagent was decomposed by addition of ice H_2O and the resulting ppt. collected by filtration.

Acid hydrolysis. W (1 mg) was dissolved in 0.2 ml *n*-BuOH–HCl (19:1) and 5 μl of a 2% (w/v) soln of ferric reagent ($(NH_4)Fe(SO_4)_2 \times 2H_2O$) in 2N HCl added. The mixt. was sealed in 1 ml glass vials and kept for 60 min at 100°. The soln was examined by TLC (Forestal), the pigment zone scraped off, eluted

and photometrically measured in 0.01% HCl–MeOH. W gave only one pigment with $R_f = 0.42$ and UV/VIS (0.01% HCl–MeOH) λ_{max} nm: 273, 536. These data were consistent with data obtained from an authentic sample for cyanidin-HCl and with lit. values [26].

Analytical, partial thiolysis. Partial thiolysis of fr. W3.3 and compounds **9** and **10** was performed as described for 'M_N determination by complete thiolysis' but the reaction time was only 10 hr (5 hr for compound **10**) at 94°. Degradation products were identified by HPLC addition analysis using the same elution conditions as described above. R_t for the cleavage products **2**, **5**, **1**, **3** and **4** were 28.0, 23.8, 8.8, 6.4 and 13.6 min, respectively. Authentic samples: **1** from Fluka AG; **3**, **4** and **7** isolated from E and unequivocally identified; **2** complete thiolysis of **3**; **5** partial thiolysis of **7**. R_t of **6** (= 27.3 min) was determined by partial thiolysis of **8**. The chain-terminating flavan-3-ols of compound **10** were analysed using the following gradient: linear from 20% to 40% A in 25 min, isocratic for 5 min, linear gradient from 40% to 100% A in 3 min, followed by washing for 17 min and reconditioning of the column. The R_t for the cleavage products **3** and **7** were 14.0 and 17.5 min, respectively.

Partial or complete, preparative thiolysis. Samples (30 mg) were dissolved in 3 ml EtOH 96%, 150 μl toluene-α-thiol and 60 μl HOAc added under N_2. The vial was sealed and kept for 10–15 hr for partial thiolysis or 24 hr for complete thiolysis at 94°. After evapn of solvent, the oily residue was flash chromatographed on MCI-gel (30 × 10 mm) with MeOH (15% → 100%, 5% steps). Thiolysis of **3** yielded **2** and **1**, thiolysis of **7** yielded **5**, **2** and a mixt. of **1**, **3** and **7**, which were separated on Sephadex LH-20 (260 × 11 mm) with EtOH 96% as eluent. Thiolysis of **8** yielded a mixt. of the thioethers **2** and **6** and a mixt. of **1**, **3** and **8**. These mixts were separated on Sephadex LH-20 (260 × 11 mm) with EtOH 96% as eluent.

(−)-Epicatechin-4β-benzylthioether (**2**). $[\alpha]_D^{26}$ −9.6° (Me_2CO; *c* 1.147) (from thiolysis of W 3.1), lit. for (+) - epicatechin - 4α - benzylthioether [23]: $[\alpha]_D^{28}$ +29° (Me_2CO; *c* 0.31). HPLC showed that smaller amounts of **5** and **6** were also present which both have positive OR values. This explains the low value for **2**. ^{1}H NMR data consistent with published values [27].

(−) - Epicatechin - [4β → 8] - (−) - epicatechin - 4β - benzylthioether (**5**). ^{1}H NMR (Me_2CO-d_6, standard acetone Me_2CO-d_5 = 2.04 ppm): δ 3.98 (1H, *br s*, H-3(u)), 4.01 and 4.06 (1H each, AB, *J* = 13.5 Hz, –S–CH_2–), 4.07 (1H, *br s*, H-3(l)), 4.13 (1H, *br d*, *J* = 1.8 Hz, H-4(l)), 4.72 (1H, *br s*, H-4(u)), 5.12 (1H, *br s*, H-2(u)), 5.32 (1H, *br s*, H-2(l)), 5.95–6.01 (3H, *br s*, H-6(u), H-8(u), H-6(l)), 6.70–6.83 (4H, *m*, H-5′(u), H-5′(l), H-6′(u), H-6′(l)), 6.96 (1H, *br s*, H-2′(u)), 7.05 (1H, *br s*, H-2′(l)), 7.23 (1H, *m*, H-4 benzyl-ring), 7.31 (2H, *m*, H-3 and H-5 benzyl-ring), 7.46 (2H, *m*, H-2 and H-6 benzyl-ring). 100 MHz ^{1}H NMR data of **5** in Me_2CO-d_6–D_2O [16] showed small differences from our data. These deviations can be attributed to the addition of D_2O and to the poorer resolution of tl 100 MHz spectrum.

(−) - Epicatechin - [4β → 6] - (−) - epicatechin - 4β benzylthioether (**6**). ^{1}H NMR (Me_2CO-d_6, standa Me_2CO-d_5 = 2.05 ppm): δ 3.99 (1H, *m*, H-3(l)), 3.98 4.06 (2H, not resolved, –S–CH_2–), 4.05 (1H, *d*, *J* = 2 Hz, H-4(l)), 4.13 (1H, *m*, H-3(u)), 4.67 (1H, *d*, *J* = 1.6 Hz, H-4(u)), 5.03 (1H, *br s*, H-2(u)), 5.23 (1H, *br* H-2(l)), 6.05 (1H, *br s*, H-8(l)), 6.09–6.11 (2H, n resolved, H-6(u), H-8(u)), 6.70–6.84 (4H, *m*, H-5′(u H-5′(l), H-6′(u), H-6′(l)), 6.98 and 7.05 (1H eac H-2′(u), H-2′(l)), 7.20–7.52 (5H, *m*, benzyl-ring 100 MHz ^{1}H NMR data of **6** in Me_2CO-d_6–D_2O [1(showed small differences from our data. These devi tions can be attributed to the addition of D_2O.

SDS–PAGE. Cholera toxin (8 μg) dissolved in 20 μ H_2O was treated for 15 min with the test sample dissolved in 10 μl H_2O. Sample buffer (30 μl, 3.2 n 0.5M Tris–HCl pH 6.8; 2.3 g glycerol 87%; 4.0 n SDS 10%; 0.5 ml Bromphenol Blue 0.4%) and 5 μ 2-mercaptoethanol were added and the mixt. kept fc 7 min at 100°. Denaturated proteins were analysed b SDS–PAGE according to ref. [28] and stained wit Coomassie-Blue. The lowest dose (μg) at which n A-band of the toxin was detectable was determined fc frs W3.1 to W3.7. The results were as follows: W3.1 7.5; W3.2: 15; W3.3: 30; W3.4: 15; W3.5: 15; W3.(15; W3.7: 15.

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REFERENCES

1. Heinrich, M., Rimpler, H. and Antonio, B. N (1992) *J. Ethnopharmacol.* **36**, 63.
2. Aguilar, A., Camacho, J. R., Chino, S., Jácquez, I and López, M. E. (1994) *Herbario Medicinal de Instituto Mexicano del Seguro Social.* Institut Mexicano del Seguro Social, Mexico D. F.
3. Hör, M., Rimpler, H. and Heinrich, M. (1995 *Planta Med.* **61**, 208.
4. Williams, V. M., Porter, L. J. and Hemingway, R W. (1983) *Phytochemistry* **22**, 569.
5. Porter, L. J. (1984) *Rev. Latinoamer. Quim.* **15**, 4
6. Nonaka, G.-I., Kawahara, O. and Nishioka, I (1983) *Chem. Pharm. Bull.* **31**, 3906.
7. Hashimoto, F., Nonaka, G.-I. and Nishioka, I (1992) *Chem. Pharm. Bull.* **40**, 1383.
8. Tanaka, T., Takahashi, R., Kouno, I. and Nonak

G.-I. (1994) *J. Chem. Soc. Perkin Trans. I*, 3013.
9. Porter, L. J., Hrstich, L. N. and Chan, B. G. (1986) *Phytochemistry* **25**, 223.
10. Haslam, E., Lilley, T. H., Cai, Y., Martin, R. and Magnolato, D. (1989) *Planta Med.* **55**, 1.
11. Cai, Y., Evans, F. J., Roberts, M. F., Phillipson, J. D., Zenk, M. H. and Gleba, Y. Y. (1991) *Phytochemistry* **30**, 2033.
12. Thompson, R. S., Jacques, D., Haslam, E. and Tanner, R. J. N. (1972) *J. Chem. Soc. Perkin Trans. I*, 1387.
13. Moumou, T., Trotin, F., Vasseur, J., Vermeersch, G., Guyon, R., Dubois, J. and Pinkas, M. (1992) *Planta Med.* **58**, 516.
14. Nonaka, G.-I., Kawahara, O. and Nishioka, I. (1982) *Chem. Pharm. Bull.* **30**, 4277.
15. Kolodziej, H. (1984) *Phytochemistry* **23**, 1745.
16. Hsu, F.-L., Nonaka, G.-I. and Nishioka, I. (1985) *Chem. Pharm. Bull.* **33**, 3142.
17. Foo, L. Y. and Karchesy, J. J. (1989) *Phytochemistry* **28**, 1743.
18. Ezaki-Furuichi, E., Nonaka, G.-I., Nishioka, I. and Hayashi, K. (1986) *Agric. Biol. Chem.* **50**, 2061.
19. Morimoto, S., Nonaka, G.-I. and Nishioka, I. (1986) *Chem. Pharm. Bull.* **34**, 633.
20. Fletcher, A. C., Porter, L. J., Haslam, E. and Gupta, R. K. (1977) *J. Chem. Soc. Perkin Trans. I*, 1628.
21. Hemingway, R. W., Foo, L. Y. and Porter, L. J. (1982) *J. Chem. Soc. Perkin Trans. I*, 1209.
22. Kolodziej, H. (1986) *Phytochemistry* **25**, 1209.
23. Geiss, F., Heinrich, M., Hunkler, D. and Rimpler, H. (1995) *Phytochemistry* **39**, 635.
24. Pallenbach, E., Scholz, E., König, M. and Rimpler, H. (1993) *Planta Med.* **59**, 264.
25. Prieur, C., Rigaud, J., Cheynier, V. and Moutounet, M. (1994) *Phytochemistry* **36**, 781.
26. Harborne, J. B. (1958) *Biochem. J.* **70**, 22.
27. Scholz, E. and Rimpler, H. (1989) *Planta Med.* **55**, 379.
28. Laemmli, U. K. (1970) *Nature* **227**, 680.
29. Hemingway, R. W. (1989) in *Chemistry and Significance of Condensed Tannins* (Hemingway, R. W. and Karchesy, J. J., eds), p. 83. Plenum Press, New York.